SERUM FERRITIN –AN INDEPENDENT PROGNOSTIC MARKER IN PREDICTING EARLY MORTALITY IN ADVANCED LIVER DISEASE

Dissertation submitted in partial fulfilment of requirements for

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CHENNAI 600003

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CERTIFICATE

This is to certify that the dissertation entitled **"SERUM FERRITIN –AN INDEPENDENT PROGNOSTIC MARKER IN PREDICTING EARLY MORTALITY IN ADVANCED LIVER DISEASE"** is a bonafide work done by **Dr. SHUJAATH ASIF.M** at Madras Medical College, Chennai in partial fulfilment of the university rules and regulations for award of D.M., Degree in Medical Gastroenterology (Branch-IV) under my guidance and supervision during the academic year 2011 -2014.

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DECLARATION

I solemnly declare that this dissertation "**SERUM FERRITIN –AN INDEPENDENT PROGNOSTIC MARKER IN PREDICTING EARLY MORTALITY IN ADVANCED LIVER DISEASE**" was done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, during 2010-2013 under the guidance and supervision of **Prof. MOHAMMED ALI M.D, D.M.** This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of D.M. Degree in Medical Gastroenterology (Branch-IV).

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ABSTRACT

INTRODUCTION

Various prognostic models were devised to predict the future events in patients with cirrhosis, thereby help in listing the patients for transplantation. Model for end stage liver disease (MELD) is one such mathematical model which was found to be accurate in predicting mortality. MELD is usually preferred for organ allocation priorities whereas CTP score is preferred in daily practice.

This study was carried out to know the efficacy of serum ferritin in predicting future events in patients with advanced liver disease.

PRINCIPAL AIM OF THE STUDY was to study whether serum ferritin can independently predict the 15 day mortality in patients with advanced liver disease.

MATERIALS AND METHODS

This study was a prospective analytical evaluation, conducted at tertiary referral center, Department of Medical gastroenterology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. The evaluation period was from June 2013 to March 2014. Adult patients in age group 12 years and above with chronic liver disease were enrolled. Demographic data, medical history, co-morbid history, drug history, anthropometric measurements and physical examination were extracted from prospective database. Routine blood investigations, liver biochemistry, metabolic work up, renal function tests, **serum ferritin levels,** relevant imaging of abdomen and upper G.I endoscopy were recorded. All the patients enrolled were followed up. Mortality was assessed at 15^{th} day of evaluation. Prognostic models along with serum ferritin were analysed.

RESULTS

A total of 75 consecutive patients were enrolled. 5 patients were excluded as 3 patients lost to follow up and 2 had HCC. Hence the total participants were 70 patients. Among the 70 patients 65 were diagnosed to have decompensated cirrhosis and remaining 5 patients were in compensated phase of cirrhosis. None

of the consecutive patients enrolled satisfied the criteria of Acute on Chronic Liver Failure. Male to female ratio was 8:1. Majority of patients (49 patients) were in 40 to 60 year age group. The clinical profile, laboratory investigations, prognostic models and outcome were looked upon. All the patients involved in the study had jaundice at the time of presentation, 66 patients (94%) had ascites. 74 % of patients had encephalopathy. Majority of them were in lower grade. Mortality was found to be increased in higher grades of encephalopathy. 60 % of the patients evaluated had experienced upper G.I bleed. Majority patients showed alcohol as the cause of liver disease, followed by HBV and NAFLD. Serum creatinine and serum sodium were found to be useful in predicting mortality. Bilirubin and transaminases were increased in all patients, but were not useful as prognostic marker. CTP score, MELD and serum ferritin were found to be useful prognostic models in predicting outcome, but serum ferritin was superior to other two models. Addition of serum ferritin to MELD was found to increase the accuracy and precision.

CONCLUSION

Serum ferritin levels were highly elevated in patients with early mortality. Serum ferritin as an independent prognostic appears to be convincing but large prospective multi-center studies should be carried out before being recommended in hepatology practice.

INTRODUCTION

INTRODUCTION

Cirrhosis may be detected in asymptomatic phase or symptomatic phase, the later presenting with complications of liver disease. Terminology used describe the above presentation is 'compensated' or 'decompensated'[1].

Decompensation refers to condition when cirrhotics present with jaundice, ascites, hepatic encephalopathy or bleeding varices. They may also present with hepatorenal syndrome, hypernatremia and spontaneous bacterial peritonitis.

Above terminologies are important for predicting prognosis and deciding treatment. 10 - Year survival in compensated cirrhotics is 50%, whereas among the decompensated, 18 month survival is 50%. Rate of decompensation is 10% among compensated liver disease patients[2]. Decompensated patients usually require liver transplantation.

Various prognostic models were devised to predict the future events, thereby help in listing the patients for transplantation. Mathematical models are used in medicine for diagnosis, predicting prognosis and deciding treatment. Mathematical models can be diagnostic models, prognostic models or simulation models. Model for end stage liver disease (MELD) is one such mathematical

model which was designed to know outcome in patients undergoing TIPS[3]. This was found to be accurate in predicting mortality in advanced liver disease[4].

Prognostic models should be statistically valid. Proportional hazards or Cox Regression analysis is the most appropriate statistical method for analysis.

Valid model should have two important features ACCURACY and PRECISION[6].

Accuracy is the ability to predict the event which matches the observed event, whereas precision is the ability to reproduce the predicted event[6].

MELD is one such accurate and precise prognostic model though there are other valid and useful ones. Child-Turcott-Pugh score is the traditional model for assessing prognosis in advanced liver disease, though not developed using statistical analysis[7].

MELD is usually preferred for organ allocation priorities whereas CTP score is preferred in daily practice[8]. As liver transplantation is the only curative therapy in patients with advanced liver disease, these models help in prioritizing the patients for transplant.

This study was carried out to know efficacy of serum ferritin in predicting future events in patients with advanced liver disease.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Fibrosis is a healing response that occurs in injured tissues. The progression of fibrosis to cirrhosis leads to various sequelae.

DEFINITION OF CIRRHOSIS

Term cirrhosis was coined by Laennec in 1826, derived from the word 'schirrous'.

Schirrous denotes orange or tawny surface of the liver seen at autopsy.

Working party for the World Health Organization (WHO) in 1978 defines cirrhosis as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules[9].

Fibrosis alone or nodule formation without fibrosis is not cirrhosis.

Causes

Etiology	**Treatment**
Viral hepatitis (B, C and D)	Antivirals
Alcohol	Abstention
NASH	Weight loss
Iron overload (HFE)	Venesection
Haemochromatosis	Venesection
Copper overload (Wilson 's disease)	Copper chelator

α 1 - antitrypsin defi ciency	Transplant
Type IV glycogenesis	Transplant
Galactosaemia	Withdraw milk and milk products
Tyrosinaemia	Withdraw dietary tyrosine. Transplant
Primary biliary cirrhosis	Transplant
Primary sclerosing cholangitis	Transplant
Hepatic venous outflow block Budd – Chiari syndrome	 Relieve main veinblock. Transplant
Heart failure	Treat Cardiac cause
Autoimmune hepatitis	Immunosuppression
Toxins and drugs, e.g. methotrexate, Amiodarone	Identify and stop

TABLE 1

LIMITATIONS IN ETIOLOGICAL CLASSIFICATION

The cause of cirrhosis is unknown in many cases, one cause may lead to many morphological patterns, and same form of cirrhosis may be caused many etiological factors.

MORPHOLOGICAL CLASSIFICATION

Size of liver 1. Normotrophic cirrhosis 2. Hypertrophic cirrhosis 3. Atrophic cirrhosis
Size of regeneration 1. Fine-nodular (granular) cirrhosis 2. Coarse-nodular (nodular) cirrhosis 3. Coarse-bulbous (lobular) cirrhosis 4. Mixed-nodular cirrhosis 5. “Smooth” cirrhosis
Structure of the fine tissue

1. Multilobular (multiacinar) cirrhosis 2. Monolobular (monoacinar) cirrhosis 3. Mixed forms
Progression of cirrhosis 1. Active (progressive) form 2. Inactive (stationary) form
Completion of cirrhosis 1. Complete form 2. Incomplete form 3. Incomplete septal cirrhosis

TABLE 2

CIRRHOSIS AND ITS CO-FACTORS

Various co- factors like age, sex, duration may lead to progression of disease.

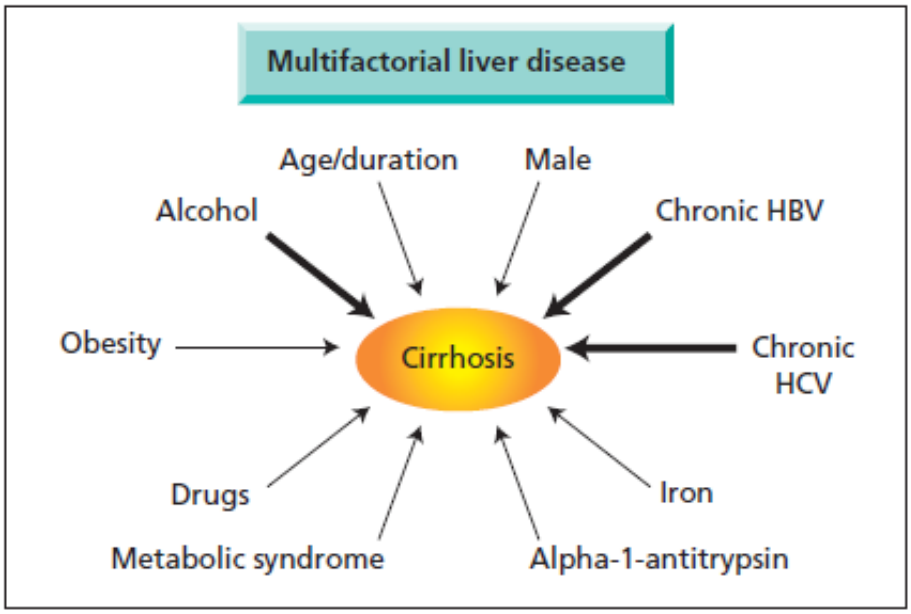


FIG 1

The above figure gives correlation between various etiologies and co-factors.

CLINICAL CLASSIFICATION

1. Latent form

2. Manifest form

    - Active form – can manifest in 2 forms 1) stage of compensation, 2) stage of decompensation
    - Inactive form

Decompensated liver disease – can have 2 forms

Portal decompensation

Metabolic decompensation

Portal decompensation
• Hypersplenism • Collateral varicosis • Portal hypertensive gastropathy • Hepatic encephalopathy • Oedema and ascites

TABLE 3

Metabolic decompensation
Jaundice • Encephalopathy • Oedema, ascites • Disturbed coagulation • Impaired protein and carbohydrate metabolism • Disturbed biotransformation • Hormonal dysbalances • Altered pharmacokinetics • Bacterial and viral infections • States of deficiency

TABLE 4

NATURAL HISTORY

Prognostic studies demonstrated that cirrhosis begins in asymptomatic state or “compensated”, which then progresses to a symptomatic or “decompensated” state, diagnosed by the presence of complications of cirrhosis such as ascites, variceal bleeding or encephalopathy. Compensated state may

present in 2 phases. The first phase will not have any varices, mortality is below 1%. In 2nd phase patient may develop varices with mortality about 3.4% per year[12].

Is cirrhosis reversible?

Fibrosis reversal has been demonstrated in number of cases. **Poynard *et al*.** showed downgradation in metavir score in patients with HCV infection with stage F4 (cirrhosis), following combination treatment with pegylated interferon and ribavarin. But it could be due sampling error during needle biopsy[10]. This is been a subject of debate as there are confounding results from various other studies.

Rat models and clinical models have demonstrated transformation from micronodular to macronodular cirrhosis with downgradation of cirrhosis.

There has been improvement in hemodynamic status as well, but no single marker has found to demonstrate the improvement[11].

FIBROSIS PROGRESSION AND HISTOLOGICAL STATES

Fibrosis develops slowly as the result of inflammation. Histologically 4 stages have been describes based on Laennec cirrhosis classification[13]. The staging is done based on fibrous bands and nodule size. Thin fibrous bands and large nodules are seen in early stage[14]. Histological stages correlate clinically and to severity of portal hypertension. Non-invasive tests like fibroscan/ transient elastography are used to demonstrate fibrosis[15].

DEVELOPMENT OF VARICES AND ITS IMPACT ON PROGNOSIS

Prevalence of varices in patients with cirrhosis is about 44%[12]. Varices develop at the rate of 5 -8 % per year in newly diagnosed cases of cirrhosis[12].

Hepatic vein pressure gradient (HVPG) measurement is useful in determining the development of varices[16]. Varices develop when HVPG is 10 mmHg or more. Average time for development of varices with or without bleed when HVPG is more than 10 mmHg is 4 years[17]. Modifying HVPG by therapies can change development and progression of varices. Size of varices is directly related to variceal bleed and mortality[16, 17, 18].

DECOMPENSATION

Cirrhotic patients decompensate at the rate of 5 % per year[19]. Incidence is twice in patients with esophagogastric varices. Factors that predict decompensation are - the model for end stage liver disease (MELD)[20], increased body mass index (BMI)[22] albumin and hepatic vein pressure gradient ≥10 mmHg[21]. Ascites is the most frequent decompensating event, followed by bleeding, jaundice, and encephalopathy[19].

MORTALITY

Mortality in asymptomatic cirrhosis is 1–3 % per year[19, 20]. It increases with development of varices. Most common cause of death is a decompensating event or liver related event.

COURSE OF DECOMPENSATED CIRRHOSIS

Patients in compensated cirrhosis can decompensate with development of ascites, bleed, jaundice and encephalopathy[19].

ASCITES AND ITS COMPLICATION

Patients with ascites usually have HVPG > 10 mm Hg[21]. Prevalence is 20 – 60% in newly diagnosed cases[23]. Ascites develops at about 5% per year in

compensated cases. Median survival after the appearance of ascites is 2 -4 years[23]. Ascites can be complicated by refractory ascites, spontaneous bacterial peritonitis and Hepatorenal syndrome[23, 24].

REFRACTORY ASCITES

Occurs in 5 -10% of cases with ascites[24]. Defined as ascites, which cannot be mobilized even after therapeutic paracentesis, salt restriction and diuretics at maximum dose.

Poor prognostic factors include low protein level in the ascitic fluid, increase in Child-Pugh score, previous history of SBP, and history of heavy alcohol consumption[25].

SPONTANEOUS BACTERIAL PERITONITIS

One of the most common infection occurring in cirrhotics[27]. SBP Accounts for 25% of all infections occurring in cirrhosis[27]. SBP occurs at the rate of 65% in patients with cirrhotics. Mortality is increased when the patients develop SBP[26, 27].

HEPATORENAL SYNDROME

HRS or functional renal failure occur when creatinine >1.5 mg/dL, not responding to plasma expansion in the absence of shock, no recent use of nephrotoxic drugs, and exclusion of parenchymal kidney disease[28].

Type I HRS has severe, rapidly progressive course where serum creatinine becomes >2.5 mg/dl in 2 weeks[28].Type II HRS has slowly progressing course[28]. Incidence of HRS is about 15% in cirrhotics and median survival is only 6 months[29].

VARICEAL BLEED

Variceal bleed occurs at rate of 5% per year[32]. Risk factors for bleed include variceal size, CTP score and red weal marks (newly formed vessels on the variceal wall) on Endoscopy[34, 34]. Bleeding stops spontaneously in 40–50 % of patients and bleeding can be controlled with therapy within 24 h from admission in nearly 85 %. Six-week mortality after variceal bleeding is 10–15 %[32, 33, 34, 35, 36].

ENCEPHALOPATHY AND JAUNDICE

Incidence of encephalopathy and jaundice is approximately 2–3 % per year. Encephalopathy can occur without ascites in the presence of spontaneous porta-caval or spleno-renal shunt. Median survival after development of jaundice or encephalopathy is 1–2 years.

HEPATOCELLULAR CARCINOMA

Incidence of HCC in cirrhosis is 70 -90 %[37, 38,38]. Hepatitis C virus (HCV) and hepatitis B virus (HBV) chronic infections constitute the most common risk factors for HCC[38, 39]. Elderly male (>55 years), increased α-fetoprotein (>20 ng/mL), and

increased BMI are the factors affecting the prognosis[38]. Survival depends on the severity of the underlying disease and the degree of portal hypertension.

Five stages of disease have been described -

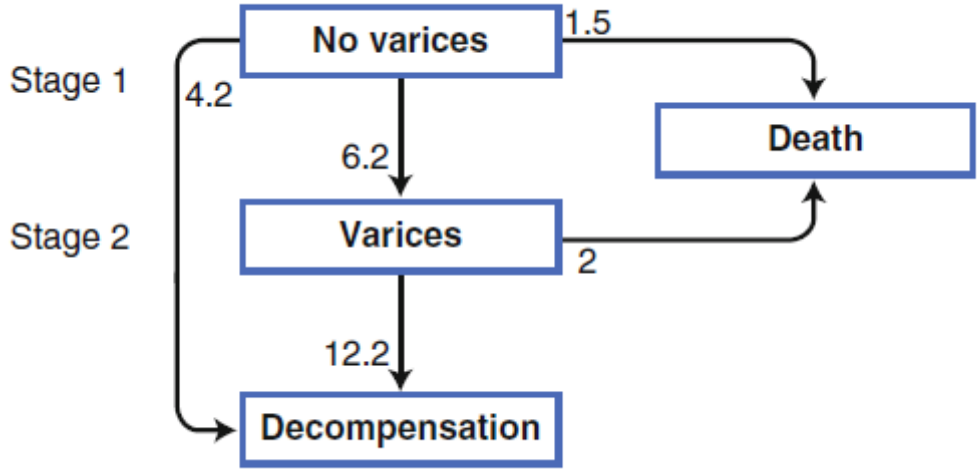


FIG 2

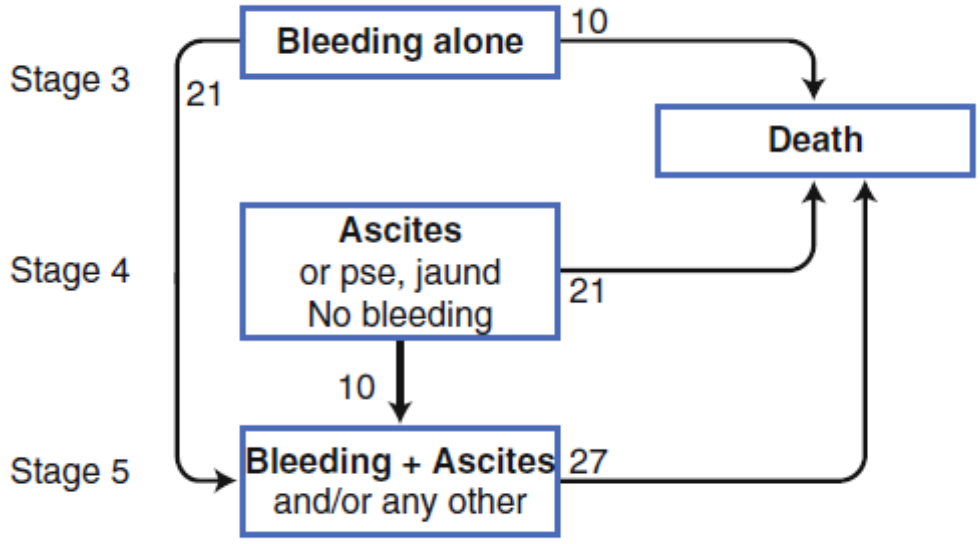


FIG 3

PROGNOSTIC INDICATORS

Child Turcott Pugh Score is traditionally used clinical prognostic model to predict short term outcome[40]. CTP SCORE, though not statistically validated, it is very useful score. CTP score depends on jaundice, ascites, encephalopathy, serum albumin and coagulopathy[40].

MELD score, a mathematical model designed to determine prognosis in patients undergoing TIPS insertion. It depends on serum creatinine, prothrombin time (INR) and serum bilirubin. MELD is very useful in determining waiting list mortality[41]. The addition of serum sodium, MELD – Na improves the accuracy and precision in predicting outcome[42].

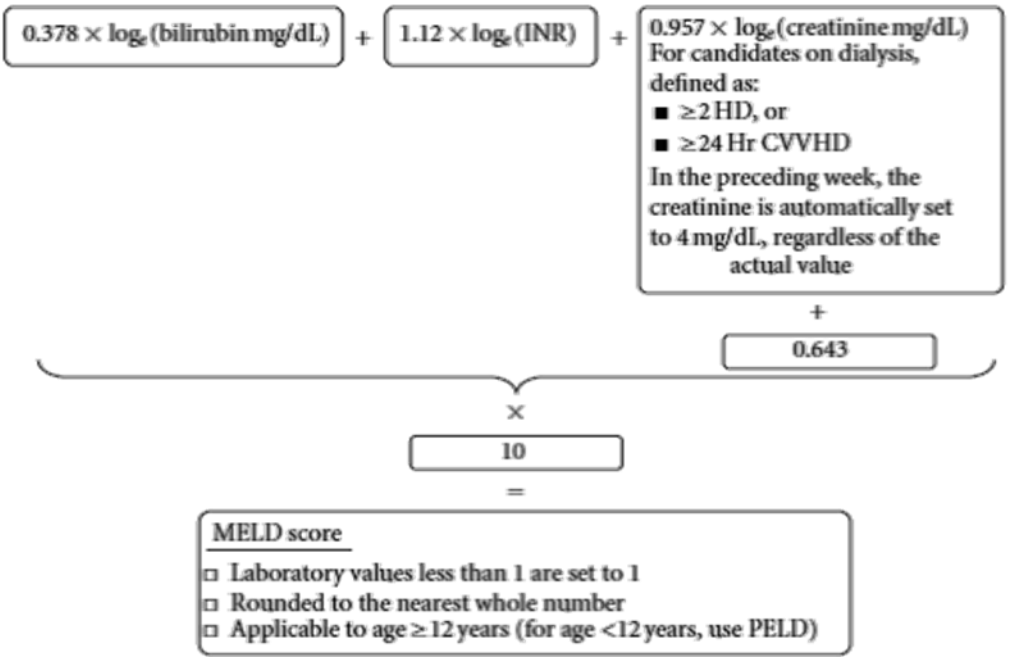


FIG 4

UKELD was developed in U.K, uses INR, serum creatinine, serum bilirubin and serum sodium. It was found to have similar accuracy and precision as MELD – Na.

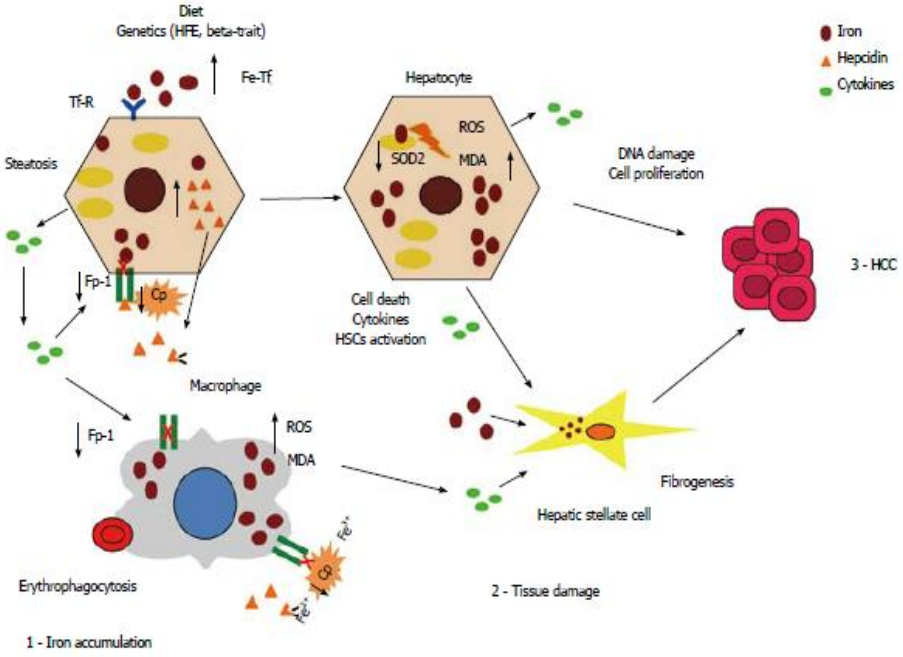
Disease - specific scoring models were found helpful in assessing mortality. Maddrey's discriminant function (MDF) determines hospital mortality and helps treatment decision in patients with alcoholic hepatitis.

It is calculated as follows:

MDF = serum bilirubin (μ mol/L)/ 17 + Prolongation of prothrombin time in seconds compared to controls × 4.6[45,46].

HVPG is also useful as independent predictor of death[44].

Serum ferritin, an acute phase reactant has shown favorable results in predicting mortality in cirrhotic patients awaiting liver transplant as an adjunct to MELD both in alcoholics and NAFLD patients[47, 48, and 49]. Hyperferritinemia was shown to associated with metabolic syndrome and plays a vital role in pathogenesis of liver injury[60]. Studies have shown that increased hepatic iron over-load is associated with increased risk of injury and progressive fibrosis[61]. Hepatic iron accumulation has been shown to be associated with HCC in NAFLD- related cirrhosis patients[62]. Animal models have also proven the mechanism of iron-dependent of cell death in pathogenesis of liver injury. This mechanism is called **Ferroptosis[63]. Role of iron in liver injury is explained in the below figure.**


Diet
Genetics (HFE, beta-trait)
Fe-Tf
Tf-R
Steatosis
Fp-1
Cp
Macrophage
Fp-1
ROS
MDA
Erythrophagocytosis
1 - Iron accumulation
Hepatocyte
ROS
SOD2
MDA
Cell death
Cytokines
HSCs activation
DNA damage
Cell proliferation
3 - HCC
Fibrogenesis
Hepatic stellate cell
2 - Tissue damage
Iron
Hepcidin
Cytokines

AIM OF THE STUDY

Aim and objectives of the study is

1. To study whether serum ferritin can independently predict the 15 day mortality in patients with advanced liver disease
2. To analyze demographic and clinical profile of patients with advanced liver disease.
3. To study predictors of 15 day mortality in patients with advanced liver disease.

MATERIALS AND METHODS

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This study was a prospective analytical evaluation, conducted at tertiary referral center, Department of Medical gastroenterology, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai. The evaluation period was from June 2013 to March 2014. Data was retrieved from prospectively enrolled medical records. Data was enrolled taking a formal informed consent. The study was approved by institute's ethics committee. No formal statistical method was applied to determine sample size.

INCLUSION CRITERIA

Adult patients in age group 12 years and above with chronic liver disease, diagnosed according to AASLD guidelines were enrolled. Patients were diagnosed to have chronic liver disease if have nodular contracted liver on ultrasound, fibrosis ≥ 2 on histology, portal vein ≥13 mm, and oesophageal varices ≥2 on endoscopy.

Adult patients in the age group 12 years and above with acute on chronic liver failure, diagnosed according to APASL guidelines were included.

TABLE 5 APASL DEFINITION FOR ACLF

Asia pacific Association of study of liver diseases (APASL) consensus guidelines
Acute hepatic insult manifesting as jaundice (serum Bilurubin = 5 mg/dL)and coagulopathy(INR = 1.5 or prothrombin activity <40%), complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease.
Working definition by EASL-AASLD on ACLF
Acute deterioration of pre-existing, chronic liver disease, usually related to a precipitating event and associated with increased mortality at 3 months due to multi-system organ failure

EXCLUSION CRITERIA

1. Age < 12 years and > 80 years.
2. Pregnant woman.
3. Patients with Hepatocellular Carcinoma.
4. Any other malignancy.
5. Patients with acute or sub-acute liver failure.
6. Patients with HIV.

METHODS

Data was extracted by enrolling consecutive patients in prospective data base. Demographic data which included age & sex, medical history, co-morbid history and drugs and native medicine history was retrieved by interviewing the patients. A physical examination including anthropometric measurements was recorded. Alcohol intake was determined from the Alcohol Use Disorders Identification Test (AUDIT-C) questionnaires.

Medical history was recorded from the patients or attendants, which included presence or absence of jaundice, ascites, confusion, oliguria and upper G.I bleed. Thorough physical exam was done and details recorded which included information like icterus, ascites, pedal edema, spider nevi, gynecomastia, abdominal wall collaterals, hepatomegaly and splenomegaly. In conscious patients mini mental status assessment was done and thorough neurological examination was done. Presence of encephalopathy was recorded and classified base on modified West Haven criteria. Liver-related events were recorded, if any during the follow up.

Blood investigations which included complete hemogram, hepatic biochemistries, metabolic labs, renal fuction tests, coagulation profile, liver

enzymes, serum ferritin (Roche electrochemiluminance assay), and serological markers for HBV and HCV were recorded. Plasma GGT, AST, and ALT were measured by Boehringer methods. Serum ceruloplasmin, immunoglobulins, autoantibodies (Nuclear, mitochondrial and smooth muscle antibodies) were done and recorded if it was found to be positive.

Presence of ascites, spontaneous bacterial peritonitis and HRS was recorded using International Ascites Club[50] and AASLD practice guidelines[51], respectively.

Imaging studies like ultra sound abdomen with Doppler, Computer tomography or MRI scans were done. Presence of HCC if any was diagnosed using radiological criteria according to AASLD guidelines. Presence of varices was identified using upper G.I endoscopy and graded according to Paquet classification.

Grade 0	No varices
Grade I	Varices, disappearing with insufflation
Grade II	Larger, clearly visible, usually straight varices, not disappearing with insufflation
Grade III	More prominent varices, locally coil-shaped and partly occupying the lumen
Grade IV	Tortuous, sometimes grape-like varices occupying the esophageal lumen

TABLE 6.PAQUET CLASSIFICATION ESOPHAGEAL VARICES

ASSESSMENT OF DISEASE SEVERITY

Maddrey's discriminant function (MDF)[45,46] was calculated for patients with alcoholic hepatitis and were classified in to groups, those with DF > 32 and with DF < 32.

DF = serum bilirubin (µ mol/L)/ 17 prolongation of prothrombin time in seconds compared to controls × 4.6

Child –Turcotte- Pugh score was calculated to assess severity of liver disease using table below.

Criteria	1	2	3
Encephalopathy	None	Grade 1 or 2	Grade 3 or 4
Ascites	None	Mild to moderate	Large or refractory to diuretics
Bilirubin (mg/dl)	<2	2-3	>3
Albumin	>3.5	2.8-3.5	<2.8
Prothrombin time (Seconds prolonged)	<4	4-6	>6
Class A 5-6 points, Class B 7-9 points, Class C 10-15 points			

TABLE 7. CTP SCORE

MELD[52] was determined to prognosticate the patient using the below - logarithmic equation. (0.957 × log [creatinine mg/dl] + 0.378 × log [bilirubin

mg/dl] + 1.120 × log [international normalized ratio] + 0.643). Patients were classified into 3 groups based MELD values and analyzes.

Patients were also classified into 3 groups based on serum Ferritin values.

GROUP A – SERUM FERRITIN < 200 ng/ml

GROUP B – SERUM FERRITIN 200 TO 400 ng/ml

GROUP C – SERUM FERRITIN > 400 ng/ml

Serum ferritin was analysed as trichotomous variable.

All the patients enrolled were followed up. Mortality was assessed at 15^{th} day of evaluation.

STATISTICAL ANALYSIS

Data was entered in Microsoft EXCEL sheet. Analysis was done using SPSS software version 20.

Normally distributed variables will be expressed as mean ± standard deviation. Differences in categorical variables between groups will be assessed using Pearson's chi-squared tests. Continuous variables were analysed by using T-test. Serum ferritin concentration will be analysed as a continuous and as a categorical variable. Kaplan-Meier survival curves will be used to show the survival in patients with high serum ferritin. Area under the receiver Operating characteristics (ROC) curves was used to analysis MELD and serum ferritin in predicting 15 day mortality. P - value < 0.05 was considered significant, if < 0.01, then highly significant

RESULTS

RESULTS

A total of 75 consecutive patients were enrolled after taking informed consent in this prospective analytical study during the study period. 5 patients were excluded because 3 patients lost to follow up and 2 had been diagnosed to have HCC.

Hence the total participants were 70 patients with advanced liver disease. Among the 70 patients 65 were diagnosed to have decompensated cirrhosis and remaining 5 patients were in compensated phase of cirrhosis. None of the consecutive patients enrolled satisfied the criteria of Acute on Chronic Liver Failure as defined by APASL.

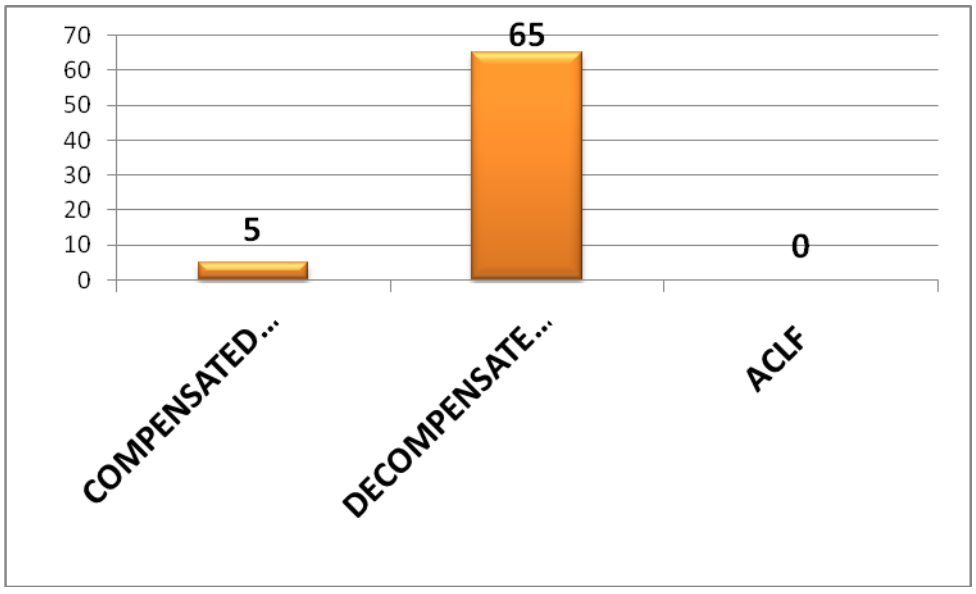


FIG 5

DEMOGRAPHIC DATA

During the evaluation of 70 patients with advanced liver disease, 62 of them were male and remaining female. Male to female ratio was 8:1.

SEX	NUMBER	PERCENT
MALE	62	88.6
FEMALE	8	11.4
TOTAL	70	100.0

TABLE 8

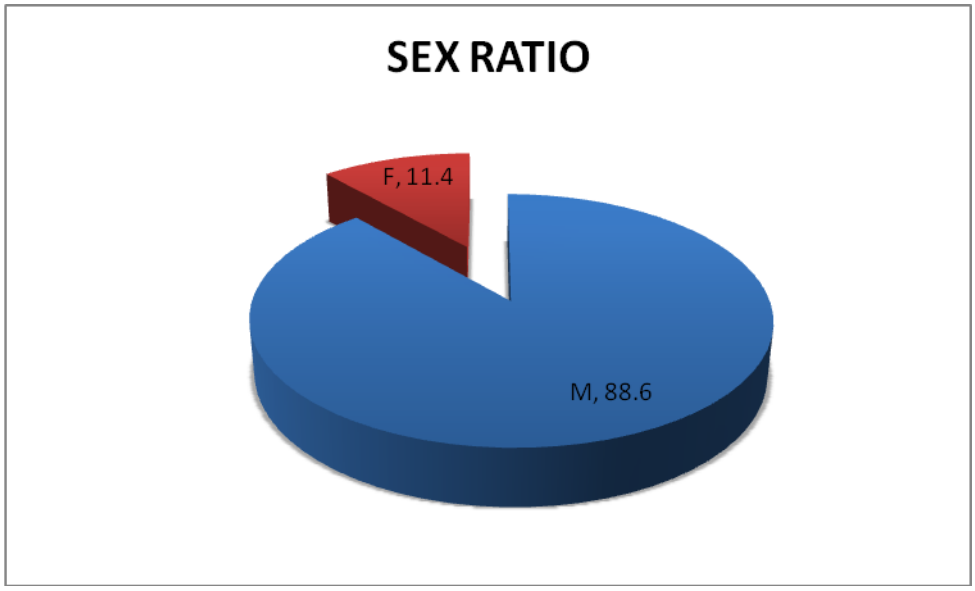


FIG 6

The mean age of patients enrolled in this prospective study was 46 years.

Majority of patients (49 patients) were in 40 to 60 year age group.

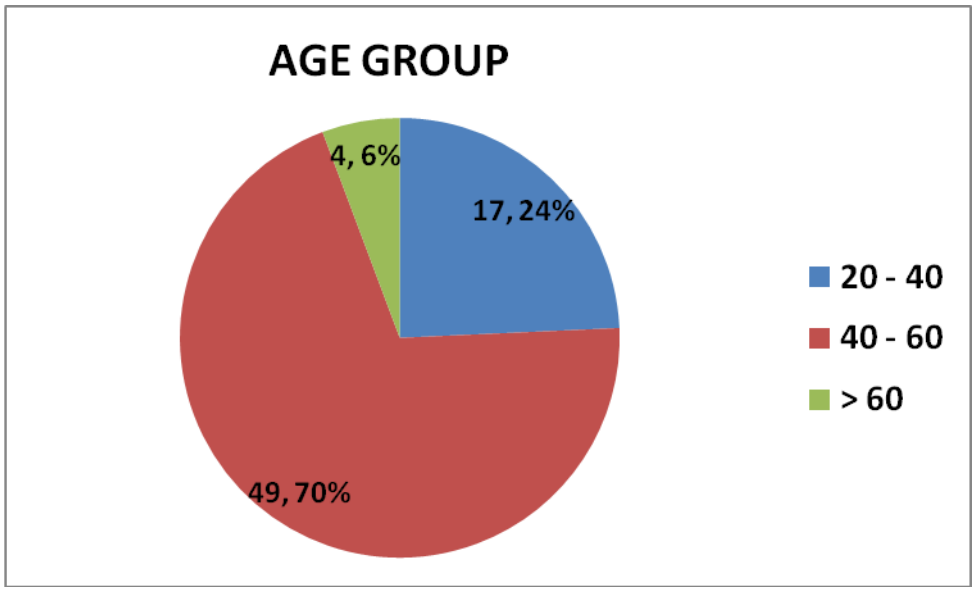


FIG 7

CLINICAL PROFILE

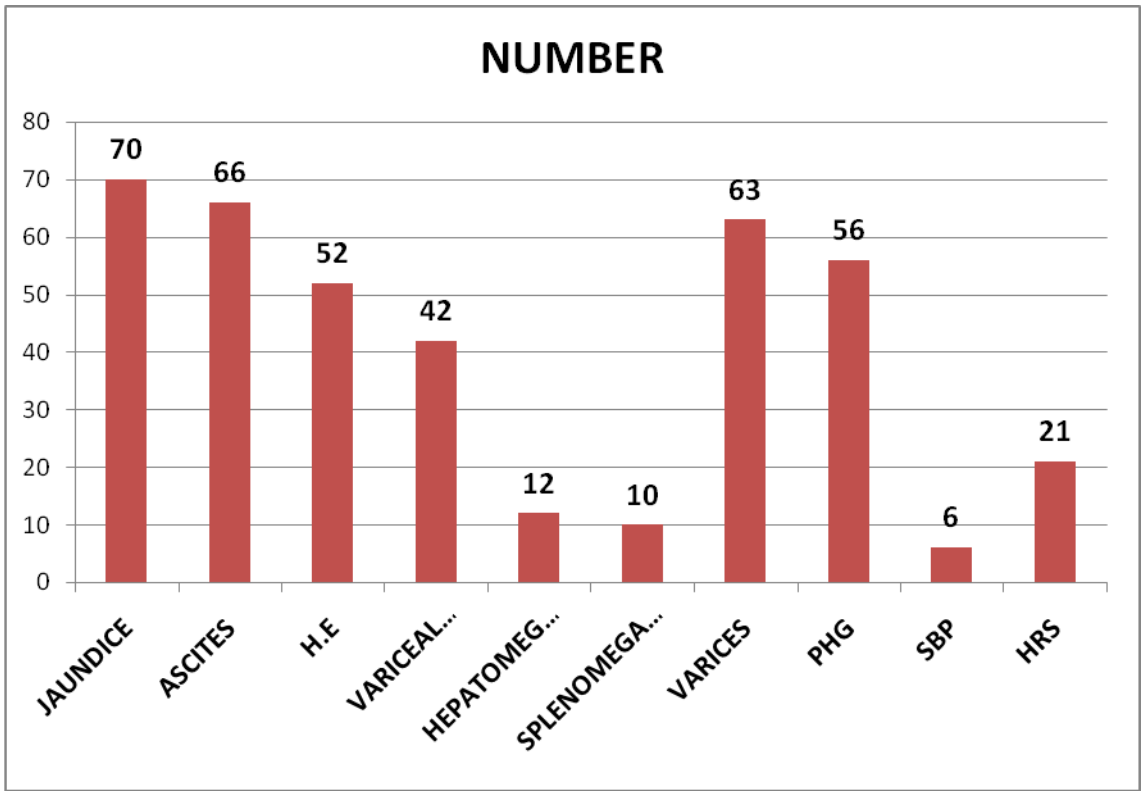


FIG 8

Among all the patients enrolled in the study all of them presented with jaundice. 66 of the patients evaluated had ascites clinically, which amounts to 94.3%. All the clinical ascites had free fluid in imaging as well.

Evaluation of clinical profile showed that 52 patients had encephalopathy, 42 variceal bleed, 12 had hepatomegaly and 10 patients had splenomegaly.

ASCITES

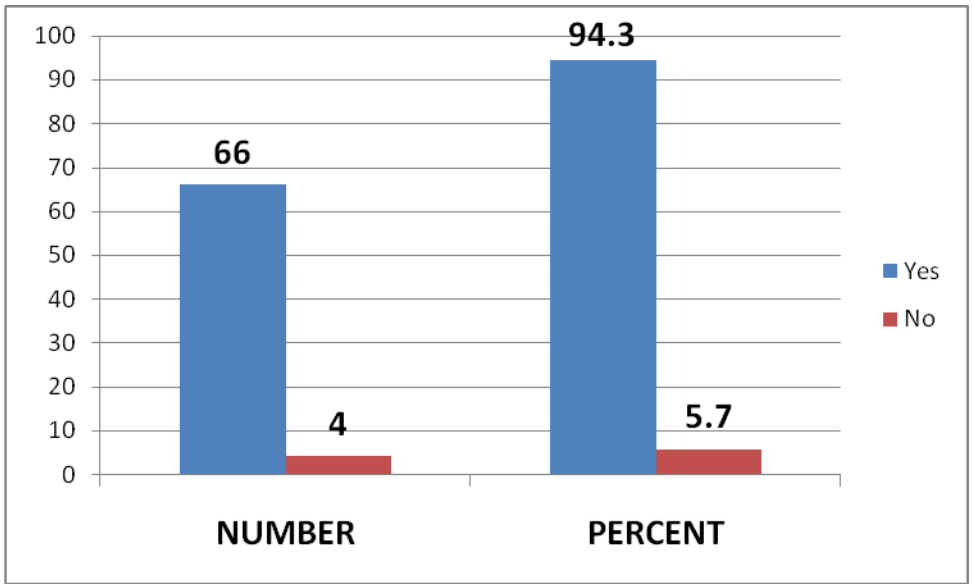


FIG 9

ENCEPHALOPATHY

Encephalopathy was diagnosed in patients enrolled with West Haven criteria.

52 patients presented with some grade of hepatic encephalopathy. 18 were found to be normal according to the criteria. Of the 52 patients with H.E, majority had grade I encephalopathy.

H.E	NO OF CASES	PERCENT
YES	52	74.3
NO	18	25.7
TOTAL	70	100.0

TABLE 9

GRADES OF H.E

H.E GRADES	NO OF CASES	PERCENT
NORMAL	18	25.7
I	24	34.3
II	1	1.4
III	17	24.3
IV	10	14.3
TOTAL	70	100.0

TABLE 10

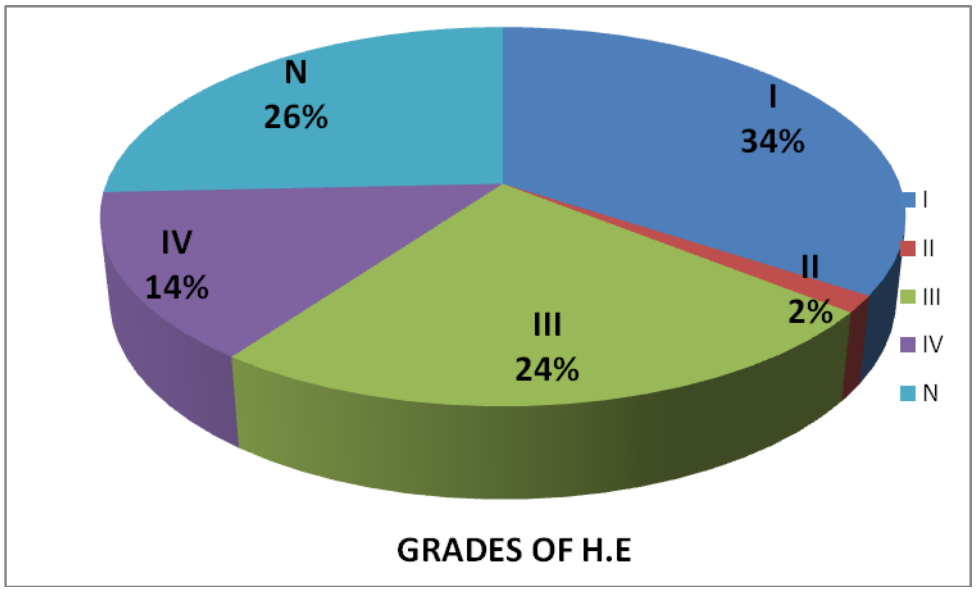


FIG 10

VARICEAL BLEED

During the study period, 42 patients enrolled experienced variceal bleed either at the presentation or during the course of evaluation.

UGI BLEED

VARICEAL BLEED	FREQUENCY	PERCENT
YES	42	60.0
NO	28	40.0
TOTAL	70	100.0

TABLE 11

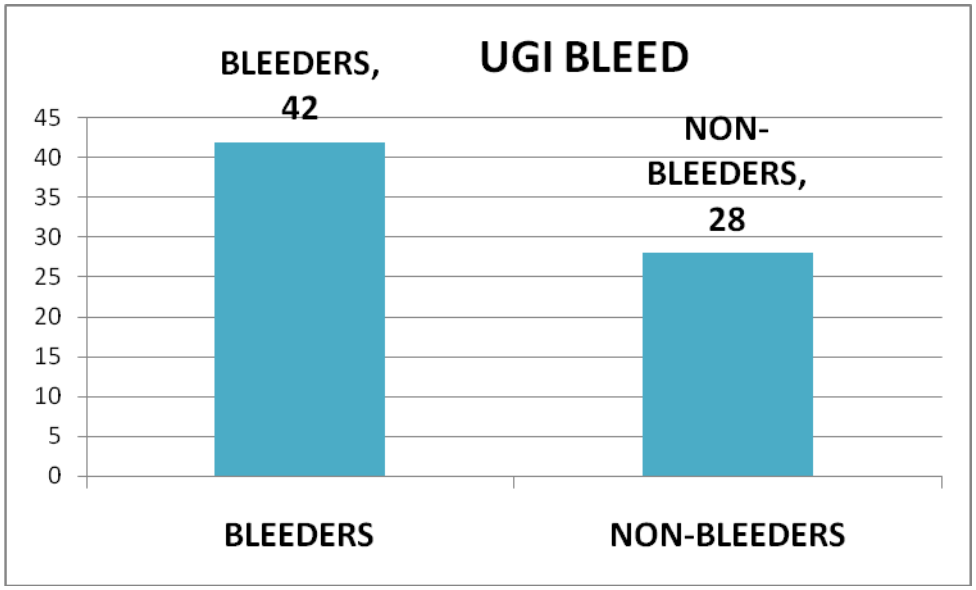


FIG 11

Among the patients analyzed, 7 were found to be diabetic during patient interview. All of them were on treatment.

33 patients had the habit of smoking and majority of them were chronic smokers.

DIABETICS	NO OF CASES	PERCENT
YES	7	10.0
NO	63	90.0
TOTAL	70	100.0

TABLE 12

SMOKERS	NO OF PATIENTS	PERCENT
YES	33	47.1
NO	37	52.9
TOTAL	70	100.0

TABLE 13

INCIDENCE OF ALCOHOLISM

Among the patients evaluated, 51 patients were alcoholics. On interviewing the patients with AUDIT – C (Alcohol Use Disorders Identification Test) Questionnaire, all of them were having cirrhogenic dose, i.e 40 to 80 gm/day for 10 years in male and 20 to 40 gm/day for 10 years in females.

Alcohol as etiology for advanced liver disease was seen in 73% of cases.

ALCOHOLICS	NO OF PATIENTS	PERCENT
YES	51	72.9
NO	19	27.1
TOTAL	70	100.0

TABLE 14

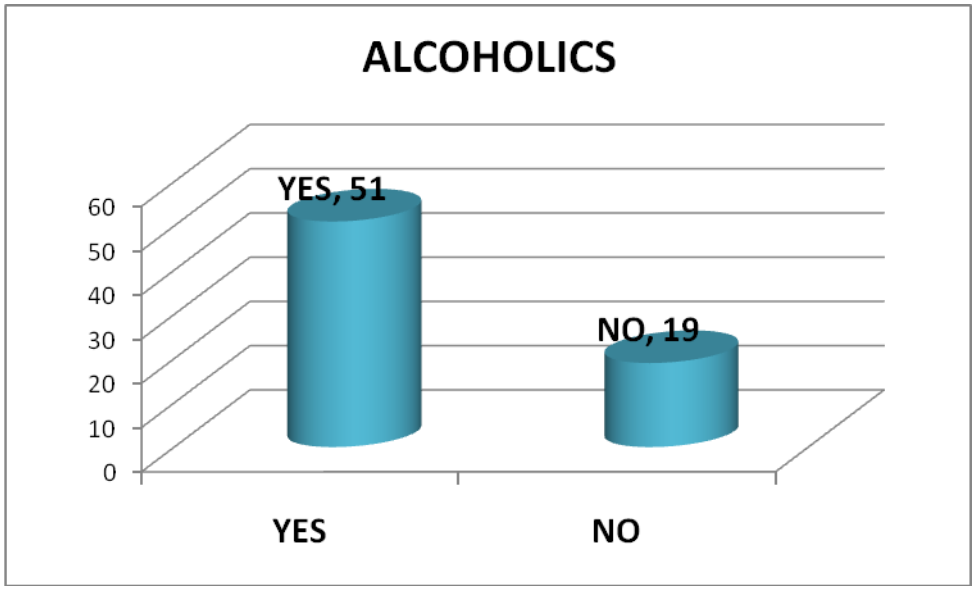


FIG 12

OTHER AETIOLOGY

Other etiological factors diagnosed in the study cases were Hepatitis B virus (HBV) alone in 9 cases, Hepatitis C virus (HCV) in 5 cases and Non-alcoholic Fatty Liver Disease (NAFLD) in 5 cases**.**

CAUSES	FREQUENCY	PERCENT
HBV	9	20.0
HCV	5	10.0
NAFLD	5	7.1

TABLE 15

HBV was diagnosed in alcoholic patients in 5 cases, 2 alcoholic patients were found to have HCV.

Majority patients showed alcohol as the cause of liver disease, followed by HBV and NAFLD.

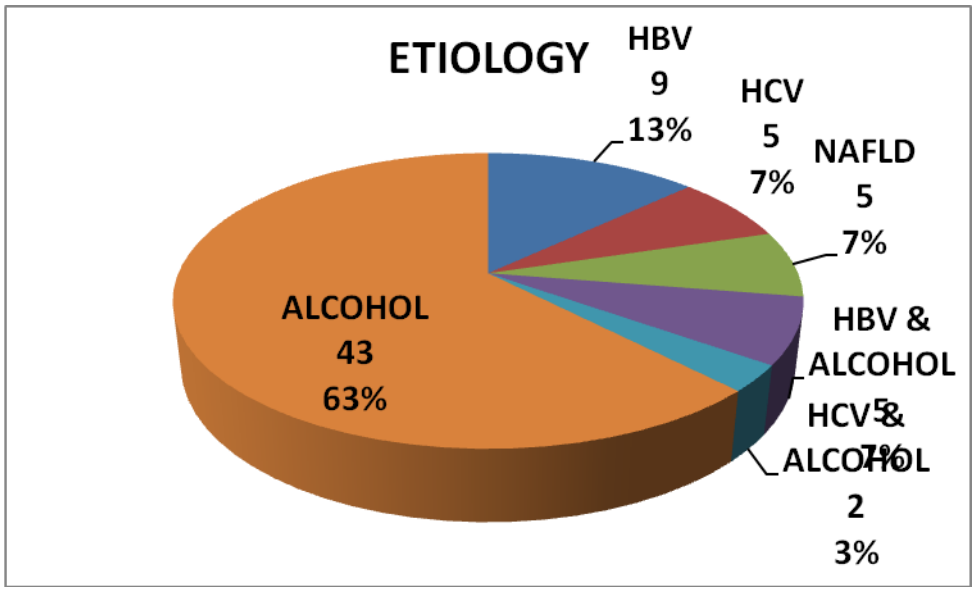


FIG 13.

10 cases with advanced liver disease enrolled in the study had splenomegaly on examination

LAB VALUES

	N	Minimum	Maximum	Mean	Std. Deviation
Age in years	70	21	67	45.91	9.603
Wbc Cells/Cu Mm	70	4300	13000	6402.29	1740.700
HB in gm%	70	2	14	8.33	2.146
Platelets lacs/cumm	70	.5	2.5	.882	.3841
RBS	70	110	245	140.67	20.389
Urea	70	20	56	28.01	7.552
Creatinine	70	.5	4.3	1.323	.9907
S.Sodium	70	111	145	136.50	8.262
S.Potassium	70	2.4	5.7	3.726	.7064
Bilurubin	70	2	26	11.41	6.755
AST	70	43	984	362.46	213.847
ALT	70	23	876	321.97	205.852
ALP	70	67	364	120.44	47.818
PROTEINS	70	5.00	7.00	5.7329	.43895
ALBUMIN	70	2.1	6.1	2.731	.6693
PT	70	13	35	22.70	5.783
INR	70	.90	3.17	1.8081	.59394
Serum ferrItin ng/ml	70	9	2654	686.97	644.983

TABLE 16

Lab investigations showed varied findings. Most of them had anemia. Causes for anemia were variceal bleed, portal hypertensive gastropathy, alcoholic gastropathy and anemia due to chronic liver disease.

White blood cell count was also found to be varied, however only 6 patients had evidence of spontaneous bacterial peritonitis. None of the patients had any other infection. Low counts could be due to hypersplenism or alcohol induced bone marrow suppression.

Majority of the patients had low platelet count; mean platelet count among the study group was 88,000/cu.mm. Cirrhosis with portal hypertension, hypersplenism and bone marrow suppression would have been the cause for thrombocytopenia in these cases.

Serum creatinine was elevated in 21 patients among 70 cases. Mean serum creatinine was 1.3.

18 patients had low serum sodium; value below 135 mg/dl was taken as cut off for hyponatremia. Mean serum sodium value 136.5 mg/dl.

10 patients in the study group had hypokalemia as well.

All the patients enrolled in the study had elevated serum bilirubin and elevated transaminases. Mean serum bilirubin, AST & ALT value were 11.4, 362 & 321 respectively. The reason for this elevation is due to loss of hepatocellular function, and all the chronic liver disease patients were in activity.

Majority of the patient had low serum albumin and abnormal coagulation profile. The mean albumin value was 2.73 and mean INR was 1.8. The above values

showed that the synthetic function of the liver was affected severely. Patients with anemia, Hb > 8 gm/dl received packed red cell transfusion. 10 patients received platelet transfusion when presented bleed and thrombocytopenia. Majority of the patients with altered renal function were managed conservatively. 6 patients underwent hemodialysis.

Patients with HRS and those with refractory ascites received albumin infusion. Fresh frozen plasma and injection vitamin K was given to patients with coagulopathy and bleed.

VARICES IN ENDOSCOPY

All the patients underwent endoscopy at some point during the study period. 63 patients had esophageal varices. 6 had gastric varices. Patients presenting with variceal bleed underwent variceal band ligation or glue injection therapy for esophageal varices and gastric varices respectively.

VARICES	FREQUENCY	PERCENT
YES	63	90.0
NO	7	10.0
TOTAL	70	100.0

TABLE 17

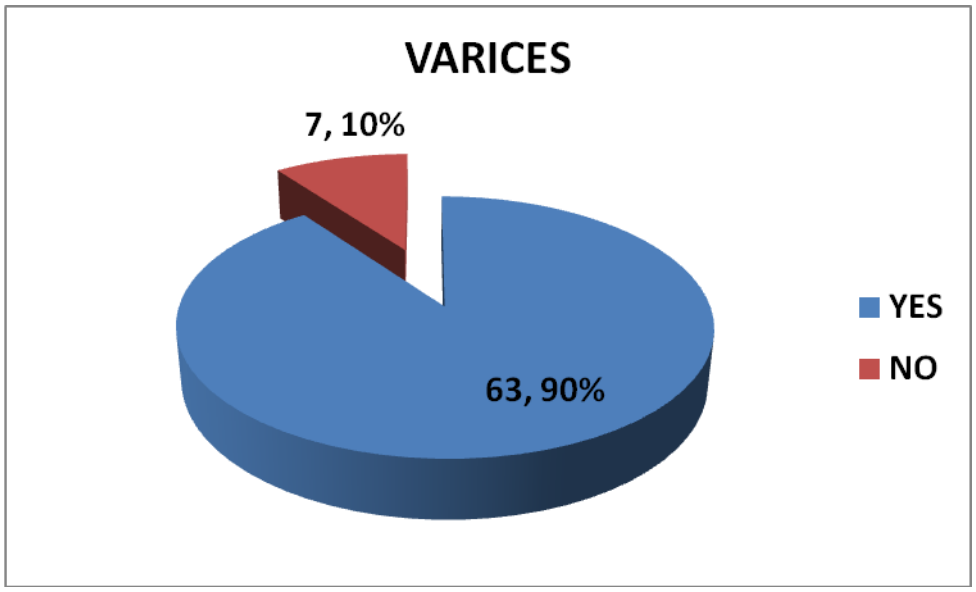


FIG 14

PORTAL HYPERTENSIVE GASTROPATHY

56 patients in our study group had portal hypertensive gastropathy.

PHG	NO OF CASES	PERCENT
YES	56	80.0
NO	14	20.0
TOTAL	70	100.0

TABLE 18

SPONTANEOUS BACTERIAL PERITONITIS

6 out of 70 patients evaluated had spontaneous bacterial peritonitis diagnosed according to AASLD practice guidelines. All of them were treated with culture sensitive antibiotics. Initially patient with suspicion of SBP were treated with empirical antibiotics.

SBP	FREQUENCY	PERCENT
YES	6	8.6
NO	64	91.4
TOTAL	70	100.0

TABLE 19

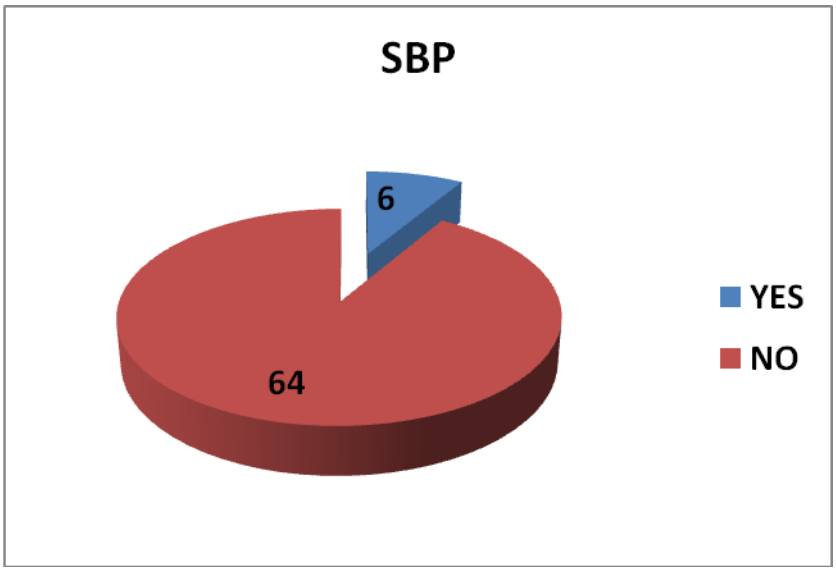


FIG 15

PROGNOSTIC SCORES

Disease specific prognostic score called Maddrey's Discriminant Fraction was calculated for patients with alcoholic hepatitis**.** Patients with DF > 32 were given pentoxyfylline. Among 50 patients with alcoholic hepatitis 44 had DF > 32.

MADDREY'S DISCRIMINANT FRACTION

D.F	NO OF CASES	Percent
M.D.F < 32	6	8.6
M.D.F > 32	44	91.4

TABLE 20

CTP SCORE

Child Turcott Pugh scores were calculated for all patients all of them were cirrhotics. Majority of the patients had CTP score more than 10 (59). 5 patients had CTP < 6 and 6 patients had score between 7 and 9.

CTP < 6	NO OF CASES	PERCENT
CTP < 6	5	7.1
CTP 7 TO 9	6	8.6%
CTP > 10	59	84%

TABLE 21

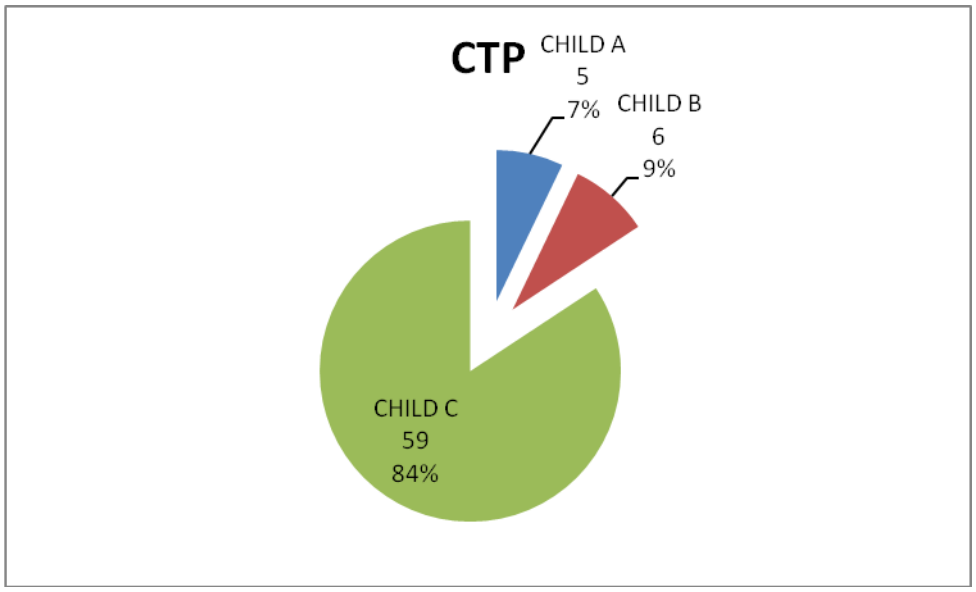


FIG 16

MELD SCORE

MELD prognostic score was calculated for all patients enrolled in study. Majority (77%) of the patients had score more than 20. 7 patients had MELD less than 9 & 8 had between 10 and 19.

MELD	NO OF CASES	PERCENT
< 9	7	10.0
10 - 19	8	11.4
> 20	54	77.1

TABLE 22

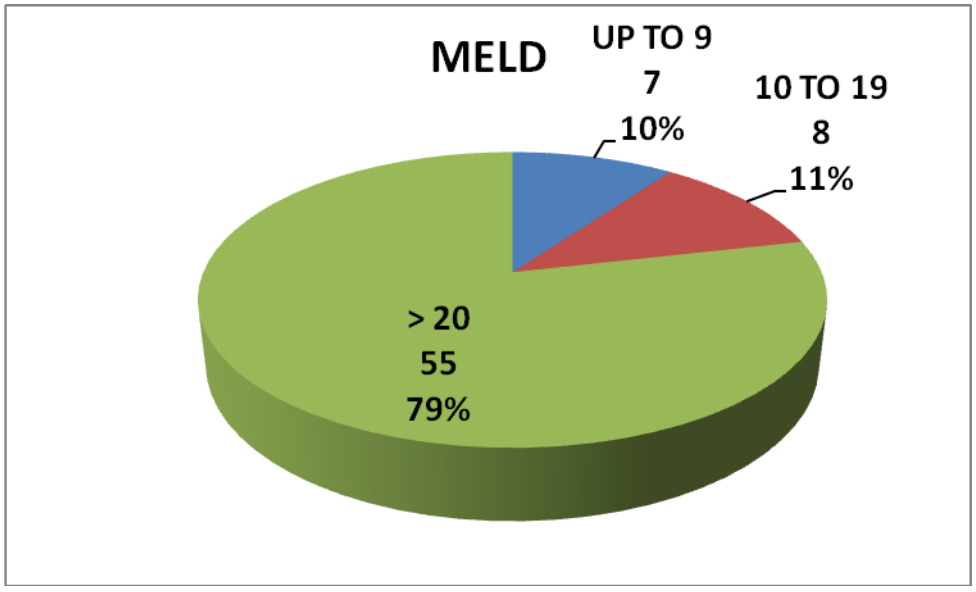


FIG 17

SERUM FERRITIN LEVELS

Serum ferritin levels were determined for all patients enrolled using Roche assay. ULN was defined as <200 ng/mL in women and <300 ng/mL in men; values were adopted from the Hemochromatosis and Iron Overload Screening Study.

Average serum ferritin value was 686 ng /ml. Maximum value was 2654 ng /ml.

Serum ferritin was analysed as trichotomous variable dividing patients into 3 groups as shown in table 25. Majority of the patients had serum ferritin levels more than 400 ng/ml as shown in table 23. Average serum ferritin levels in patients with early mortality was 1071 ng /ml and average level in patients who survived for more than 15 days was 363.47.

SE. FERRITIN IN NG/ML	NO OF CASES	PERCENT
< 200	17	24.3
200 – 400	17	24.3
> 400	36	51.4

TABLE 23

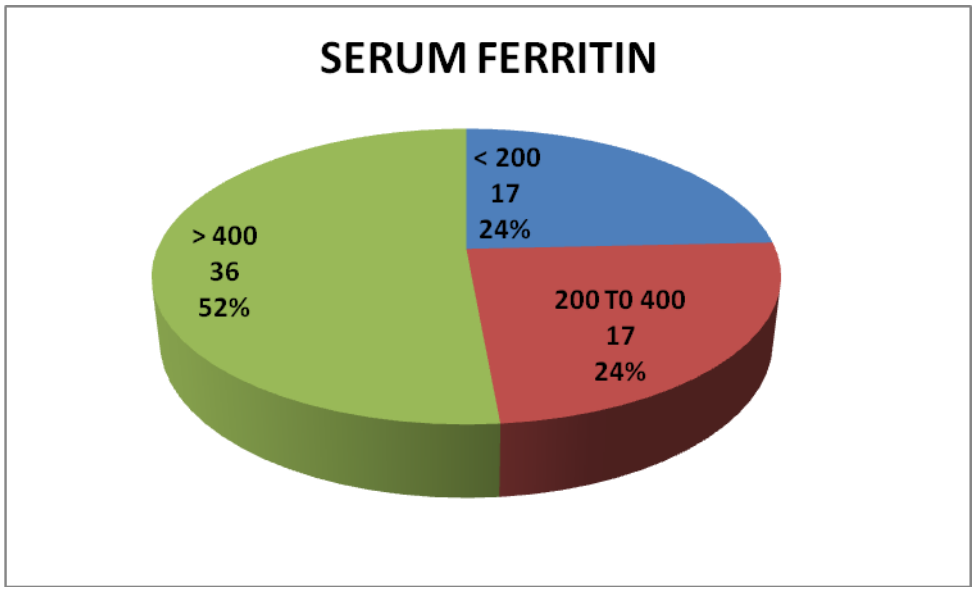


FIG 18

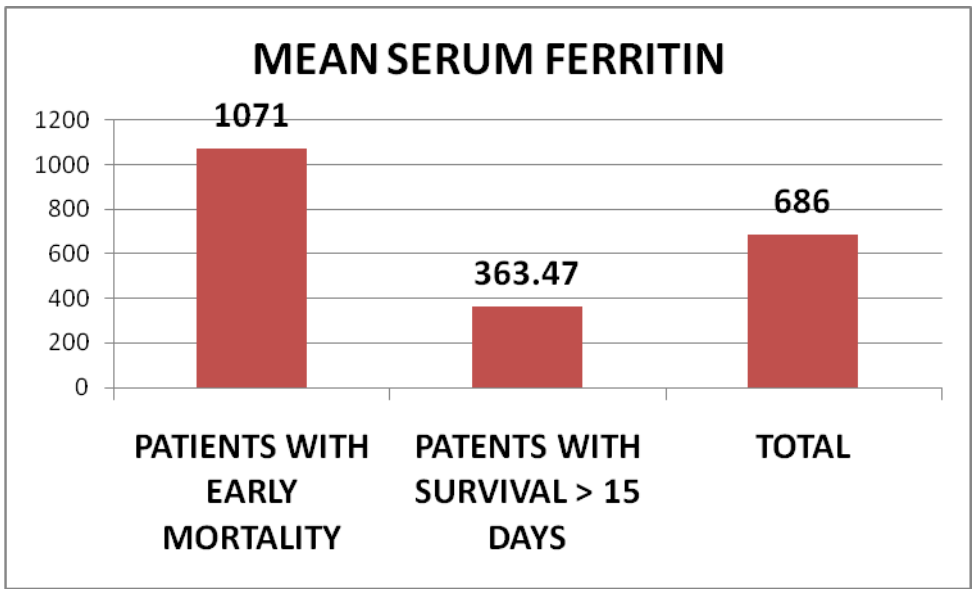


FIG 18.1

OUTCOME

All 70 patients were followed up and the mortality was assessed on 15th day of evaluation during follow up. 31 patients had survival duration less than 15 days, which accounts to 44.3 %.

OUTCOME AT 15 DAYS	FREQUENCY	PERCENT
ALIVE	39	55.7
DEATH	31	44.3
TOTAL	70	100.0

TABLE 24

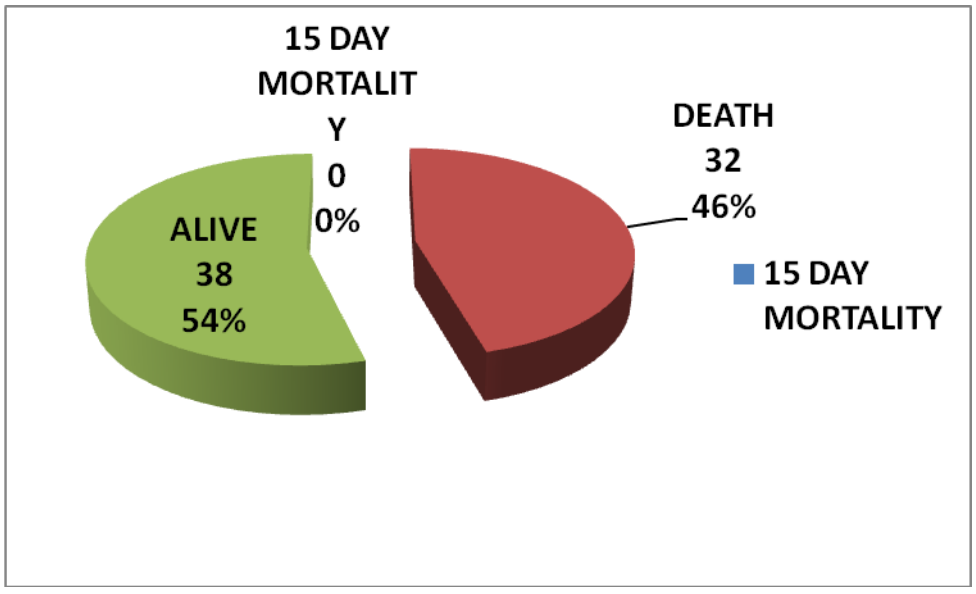


FIG 19

SERUM FERRITIN LEVELS AND OUTCOME

Serum ferritin was analysed a trichotomous variable. Analysis showed 17 patients had serum Ferritin less than 200 ng / ml. Among the 17 patients, only 1 patient had early mortality. There were 17 patients with serum Ferritin in the range, 200 to 400 ng / ml and 2 patients in this group had early mortality. Majority of the patients had serum ferritin value above 400 ng / ml. 29 patients out of 36 patients in this group had early mortality. Serum ferritin was assessed as a categorical variable using Pearson's Chi – square test. It was found to be highly significant **P Value < 0.001**, as shown in table 25 and 26.

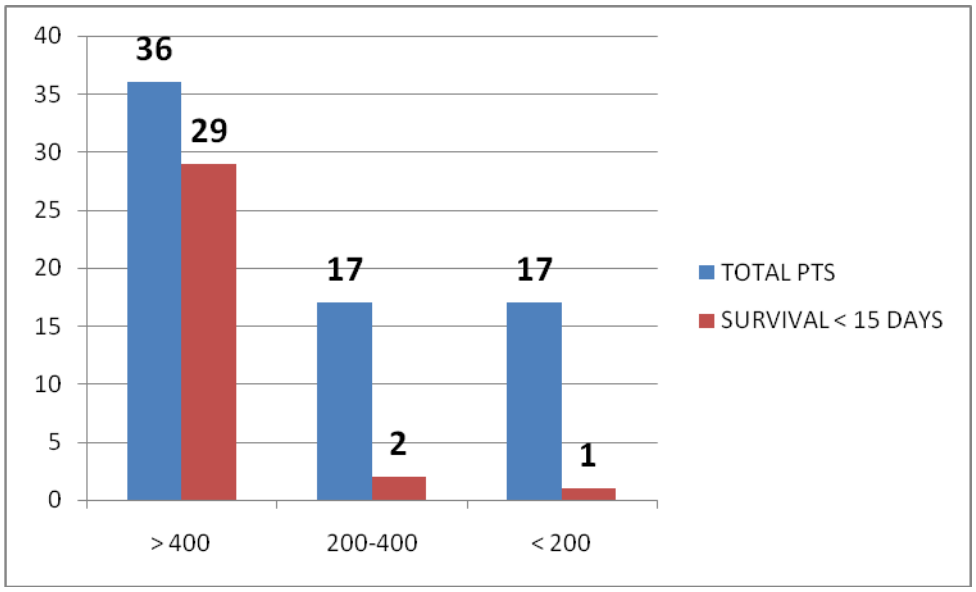


FIG 20

			Early Mortality		
			< 15	> 15	Total
Serum Ferritin	< 200	Count	1	16	17
		% within Serum Ferritin	5.9%	94.1%	100.0%
		% within Early Mortality	3.1%	42.1%	24.3%
	200-400	Count	2	15	17
		% within Serum Ferritin	11.8%	88.2%	100.0%
		% within Early Mortality	6.3%	39.5%	24.3%
	> 400	Count	29	7	36
		% within Serum Ferritin	80.6%	19.4%	100.0%
		% within Early Mortality	90.6%	18.4%	51.4%
Total		Count	32	38	70
		% within Serum Ferritin	45.7%	54.3%	100.0%
		% within Early Mortality	100.0%	100.0%	100.0%

TABLE 25

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	36.374 (a)	2	.000
Likelihood Ratio	41.137	2	.000
Linear-by-Linear Association	30.971	1	.000
N of Valid Cases	70		

TABLE 26

KAPLAN –MEIER SURVIVAL CURVES

Kaplan – Meier survival curve analysis showed patients with high serum ferritin levels had increased early mortality.

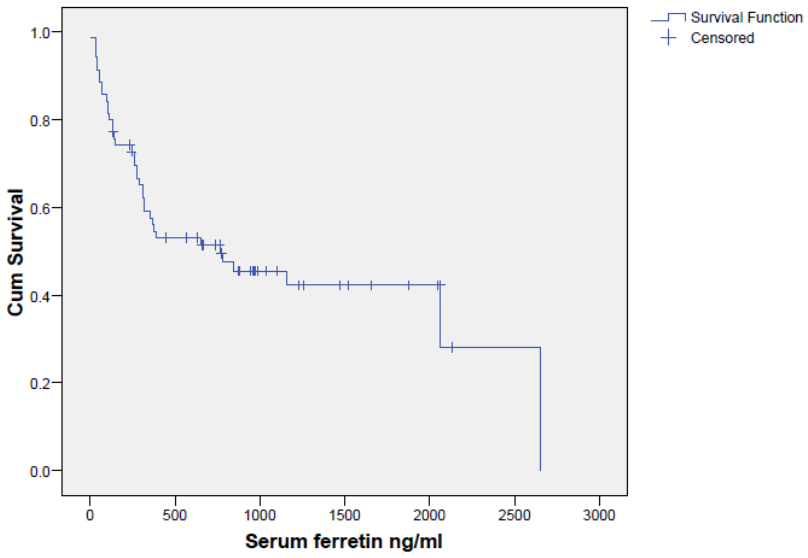


FIG 2

CTP SCORE AND OUTCOME

CTP score divided in to traditional 3 groups and assessed as a trichotomous variable using non-parametric Pearson's Chi square test. Patients with CTP score less than 6 and group of patients with CTP score between 7 and 9 had no early mortality. In other words they survived for more than 15 days. Patient group with CTP score > 10 had 54.2 % early mortality, 45.8 % survived more than 15 days. This was also highly significant, **P Value < 0.005**, as shown in table 27 and 28.

			EARLY MORTALITY		
			< 15	> 15	TOTAL
CTP	< 6	COUNT	0	5	5
		% WITHIN CTP	.0%	100.0%	100.0%
		% WITHIN EARLY MORTALITY	.0%	13.2%	7.1%
	7-9	COUNT	0	6	6
		% WITHIN CTP	.0%	100.0%	100.0%
		% WITHIN EARLY MORTALITY	.0%	15.8%	8.6%
	> 10	COUNT	32	27	59
		% WITHIN CTP	54.2%	45.8%	100.0%
		% WITHIN EARLY MORTALITY	100.0%	71.1%	84.3%
TOTAL		COUNT	32	38	70
		% WITHIN CTP	45.7%	54.3%	100.0%
		% WITHIN EARLY MORTALITY	100.0%	100.0%	100.0%

TABLE 27

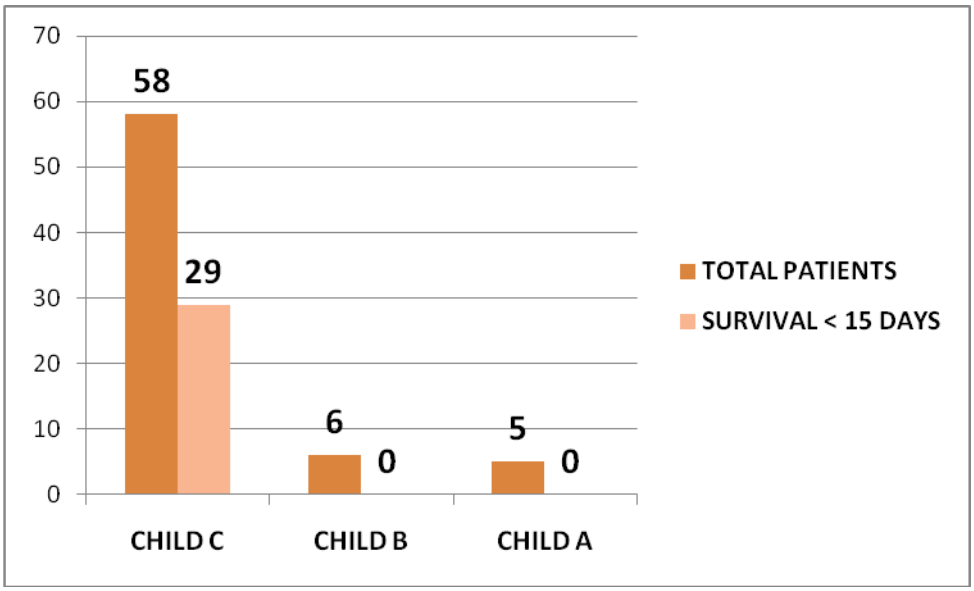


FIG 22

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.990(a)	2	.004
Likelihood Ratio	15.159	2	.001
Linear-by-Linear Association	9.511	1	.002
N of Valid Cases	70		

TABLE 28

MELD AND OUTCOME

Calculated MELD analysed by dividing the patients in to 3 group, as trichotomous variable. Again Pearson's Chi square test was used analyse the categorical variable. It was found that out of 55 patients in high MELD group, 32 had early mortality, which was 58.2 %. 8 patients had MELD between 10 and 19. No early mortality seen in this group. In group of patient with MELD < 9, no early mortality seen, this correlation was highly significant, **P Value < 0.001** as shown in table 29 and 30.

			EARLY MORTALITY		
			< 15	> 15	TOTAL
MELD	< 9	COUNT	0	7	7
		% WITHIN MELD	.0%	100.0%	100.0%
		% WITHIN EARLY MORTALITY	.0%	18.4%	10.0%
	10-19	COUNT	0	8	8
		% WITHIN MELD	.0%	100.0%	100.0%
		% WITHIN EARLY MORTALITY	.0%	21.1%	11.4%
	> 20	COUNT	32	23	55
		% WITHIN MELD	58.2%	41.8%	100.0%
		% WITHIN EARLY MORTALITY	100.0%	60.5%	78.6%
TOTAL		COUNT	32	38	70
		% WITHIN MELD	45.7%	54.3%	100.0%
		% WITHIN EARLY MORTALITY	100.0%	100.0%	100.0%

TABLE 29

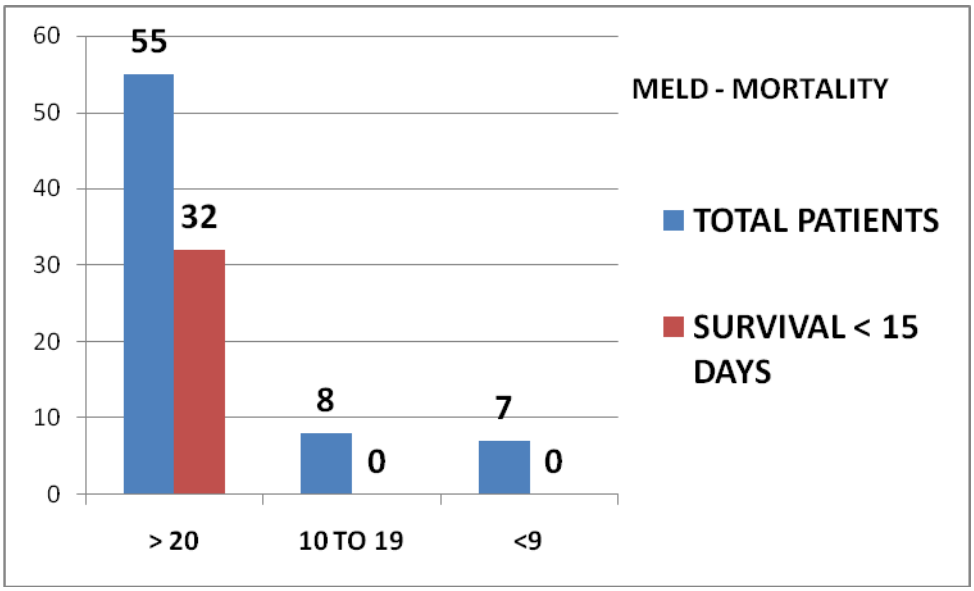


FIG 23

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	16.077(a)	2	.000
Likelihood Ratio	21.759	2	.000
Linear-by-Linear Association	13.813	1	.000
N of Valid Cases	70		

TABLE 30

	Early Mortality	N	Mean	Std. Deviation	Std. Error Mean
Sodium	**< 15**	**32**	**132.38**	**10.067**	**1.780**
	> 15	**38**	**139.97**	**3.908**	**.634**

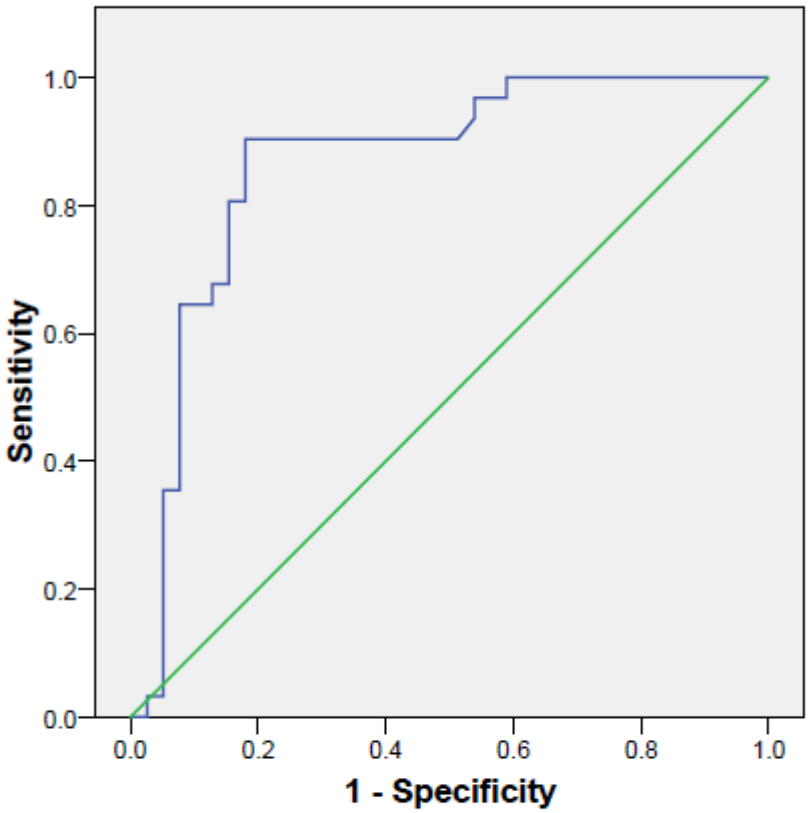
TABLE 31

Our study group patients also had subnormal serum sodium levels. Mean serum sodium was 136.5 mg/dl. In patients with early mortality mean serum sodium was 132.38 mg/dl. Serum sodium levels were analysed as independent prognostic marker using T-test. It was found to be highly significant, **P Value < 0.001**.

ROC CURVE ANALYSIS

ROC Curve analysis of 15-day mortality was done to assess if serum ferritin alone or serum ferritin in addition to MELD improved the prediction of mortality when compared to MELD alone.

ROC CURVE ANALYSIS FOR SERUM FERRITIN



Diagonal segments are produced by ties.

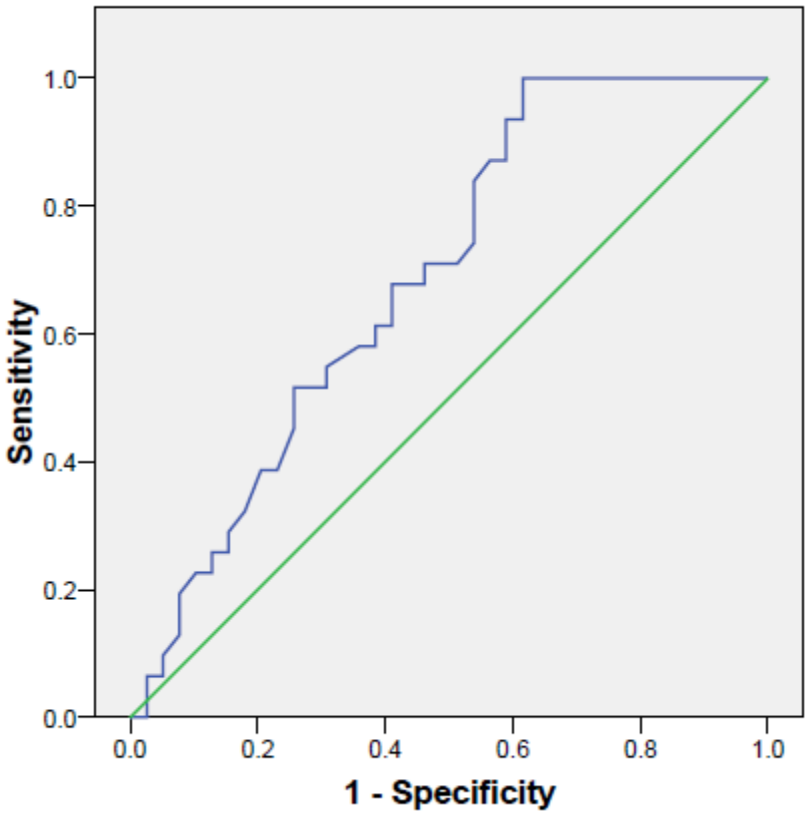
FIG 24

Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.866	.046	.000	.775	.956

AUROC for serum ferritin is .866

ROC CURVE ANALYSIS MELD

FIG 25



Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.689	.063	.007	.566	.811

AUROC for MELD IS .689. This was found to be statistically significant.

ROC CURVE ANALYSIS FOR SERUM FERRITIN + MELD

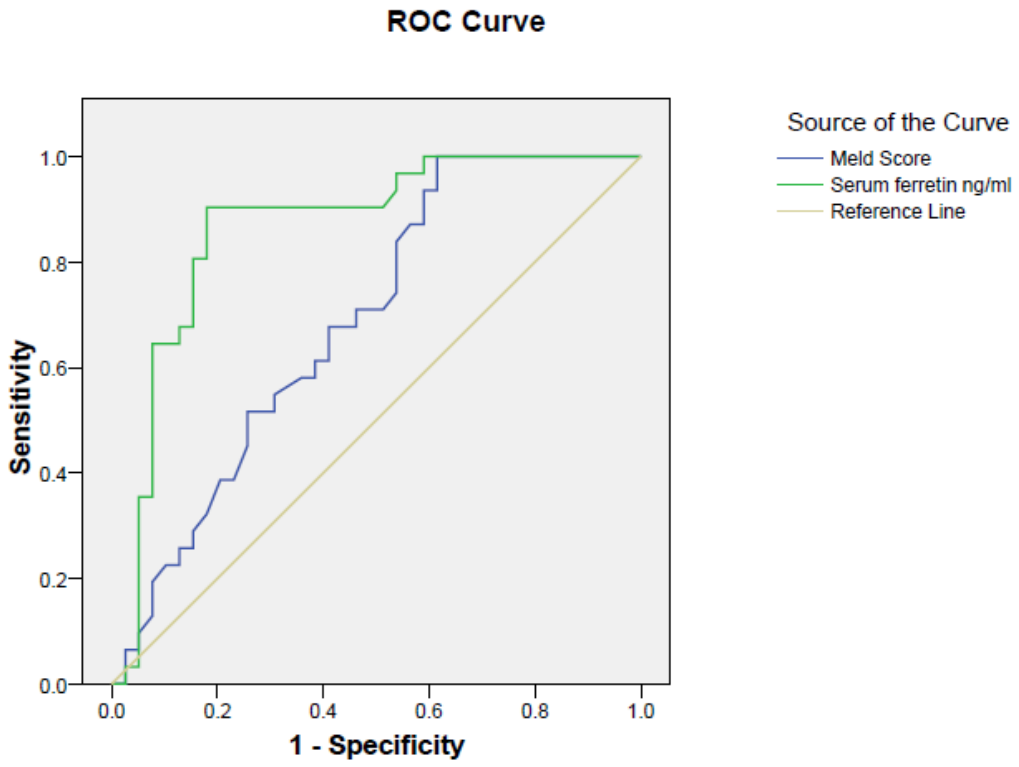


FIG 26

Test Result Variable(s)	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Meld Score	.689	.063	.007	.566	.811
Serum ferrltin ng/ml	.866	.046	.000	.775	.956

ROC CURVE analysis for serum ferritin in addition to MELD has increased the Area Under Curve by 20 % from .689 to .866. this was found statistically significant .

DISCUSSION

DISCUSSION

Various studies were conducted to evaluate the usefulness of serum Ferritin as prognosticating factor in patients with advanced liver. Results were found to be conflicting. **Skikne et al**., 1990 showed direct correlation between body iron stores and serum ferritin. Serum ferritin also increases because of liver injury, inflammation, infection and malignancy. Patients with alcoholic liver disease and NAFLD have been shown to have increased body iron stores and increase release of ferritin following liver injury and decreased clearance from circulation, thereby increasing the baseline serum ferritin values. 30 % of patients with cirrhosis found to have increased ferritin independent of HFE mutations[53 & 54.] Moreover ferritin is found to be a pro-inflammatory cytokine involved in inflammatory process causing liver injury[55]. Possibly direct relation between serum ferritin and inflammatory activity in liver is the cause of early mortality.

This is a prospective analytical study conducted at tertiary referral center in southern part of India, to analyse the usefulness of serum ferritin, a non-invasive prognostic marker of liver disease. 70 consecutive patients with cirrhosis were in this study. The clinical profile, laboratory investigations, prognostic models and outcome were looked upon.

All the patients involved in the study had jaundice at the time of presentation, 66 patients (94%) had ascites. 74 % of patients had encephalopathy. Majority of them were in lower grade. Mortality was found to be increased in higher grades of encephalopathy. None of the patients had fever any time during the study period.

60 % of the patients evaluated had experienced upper G.I bleed at some point during the duration of study. 10 % of the patients were diabetic and were on treatment.

On interviewing the patients, it was found that 73 % of the patients were alcoholic and 47 % were smokers. All of them were having cirrhogenic dose of alcohol, i.e 40 to 80 gm/day for 10 years in male and 20 to 40 gm/day for 10 years in females.

Alcohol as etiology for advanced liver disease was seen in 73% of cases, the most common cause of cirrhosis in the study group.

Other etiological factors diagnosed in the study cases were Hepatitis B virus (HBV) alone in 9 cases, Hepatitis C virus (HCV) in 5 cases and Non-alcoholic Fatty Liver Disease (NAFLD) in 5 cases**.**

HBV was diagnosed in alcoholic patients in 5 cases, 2 alcoholic patients were found to have HCV. Majority patients showed alcohol as the cause of liver disease, followed by HBV and NAFLD.

Similar study done by **Walker et al** showed viruses as the most common cause of cirrhosis[49]. Few studies have shown alcohol as the most common etiology followed by viral hepatitis. This finding could be due referral bias, as our hospital gives free treatment for poor patients.

Analysis of laboratory values showed very low average haemoglobin (8.3 gm/dl) and platelet count (80,000/cu.mm).

Anaemia could have been due to variceal bleed, portal hypertensive gastropathy, alcoholic gastropathy and anemia due to chronic liver disease. Reason for low platelet count could be due to portal hypertension and hypersplenism.

Mean creatinine in this group of patients was 1.3. Patients with early mortality had high serum creatinine. Using multiple linear regression analysis in SPSS software, serum creatinine was shown to be independent prognostic factor in above patients.

All the patients had high serum bilirubin; mean bilirubin value was 11.4 mg/dl.

Transaminases were also found be high, mean ALT value was 362.46 IU/L and mean AST was 321.97 IU/L.

Walker et al[49] showed similar findings in study.

These finding support the on-going necroinflammatory activity in the study patients. Above finding is also supported by increased mean serum ferritin value. As already discussed ferritin is a pro-inflammatory cytokine, which is released from liver when there is necro - inflammation[55].

Mean serum bilirubin value and transaminase levels in patients with early mortality were high when compared to survivors.

Our study group patients also had subnormal serum sodium levels. Mean serum sodium was 136.5 mg/dl. In patients with early mortality, mean serum sodium was 132.38 mg/dl. Serum sodium levels were analysed as independent prognostic marker using paired T - test. It was found to be highly significant.

Kim et al[42] showed hyponatremia as an independent marker of mortality and addition of sodium to MELD increased the accuracy in predicting early mortality.

CTP score was analysed in patients with early mortality and survivors, it was found that, patients with high CTP score had significantly increased early mortality.

Similarly MELD score was analysed in patients with early mortality, patients with high MELD score also had increased early mortality, which was highly significant

statistically. These findings were in accordance to the finding shown by two landmark studies.

Infante – Rivard et al[40] analysed the prognostic markers in cirrhotic patients, showed patients with high CTP scores had poor prognosis and required early transplant.

Olthoff et al[41] showed patient with cirrhosis should be allotted organs based on MELD score in adults and PELD score in children, as patients with high score had increased early mortality.

Serum ferritin levels measured in the study showed elevated mean value 686 ng/ml. Mean value of serum ferritin in patients with early mortality was high, 1071.04 ng/ml.

Serum ferritin was analysed as a trichotomous variable diving into 3 groups and patient group with high serum ferritin had high early mortality, this was statistically highly significant.

ROC curve analysis for 15 day mortality showed that serum ferritin is better than MELD in predicting mortality. Addition of serum ferritin to MELD further improves the predictability. This was also highly significant statistically.

In similar study by **Walker et al**[49] in patients awaiting liver transplant, showed high mortality in patients with high serum ferritin.

Walker et al[49] also demonstrated that, ROC curve analysis of serum ferritin and MELD in predicting mortality was better than MELD alone, but it was not statistically significant.

Manousou et al[55] showed high serum Ferritin predicts fibrosis and inflammation in NAFLD patients.

Similar finding was shown by **Knowdley et al**[58].

But the conflicting evidence was given by **Chandok et al**[59], they found that the base line ferritin levels were high in NAFLD patients but did not predict the severity of liver disease.

Vagu C et al[57] also showed that serum iron markers were useful as predictors of severe liver injury in chronic Hepatitis C patients.

CONCLUSION

CONCLUSION

Serum ferritin levels are highly elevated in patients in with advanced liver disease. It is demonstrated to be the marker of increased hepatic iron load and necroinflammatory activity. Levels are elevated due increased release from liver cell and decreased removal from circulation.

This prospective analytical study done in tertiary referral center in south India has shown that the most common cause for cirrhosis is alcohol. All patients included in the study had high bilirubin and elevated transaminases. They were found to be not useful in predicting mortality. Serum creatinine and serum sodium levels were found to be useful in predicting the outcome of patients with liver disease.

Serum ferritin levels were highly elevated in patients with early mortality. It was found to be highly accurate in predicting early mortality in cirrhotic patients. MELD score was also found to useful in predicting the outcome of patients with advanced liver disease, but serum ferritin was found to be superior in predicting mortality.

Serum ferritin as an independent prognostic appears to be convincing but large prospective multi-center studies should be carried out before being recommended in hepatology practice.

BIBILIOGRAPHY

BIBLIOGRAPHY

1. McCormick PA , Nolan N . Palpable epigastric liver as a signof cirrhosis.A prospective study.*Eur. J. Gastro. Hepatol.*2004 ;**16** : 1331 – 1334 .

2. GinesP , Quintero E , Arroyo V *et al.* Compensated cirrhosis:natural history and prognostic factors . *Hepatology*1987 ;**7** :122 – 128 .

3. Malinchoc M, Kamath PS, Gordon FD *et al*. (2000) A model to predictpoor survival in patients undergoing transjugular intrahepatic portosystemicshunts. *Hepatology*31(4), 864–871.

4. Kamath PS, Wiesner RH, Malinchoc M et *al*. (2001) A model to predict survival in patients with end-stage liver disease. *Hepatology*33(2), 464–470.

5. Collet D (1994) Modeling survival data in medical research. In:Chatfield C, Zidek JV (eds) *Texts in Statistical Science*. London: Chapman & Hall, pp. 53–106.

6. Child C, Turcotte J (1964) Surgery and portal hypertension. In:Child C (ed) *The Liver and Portal Hypertension.* Philadelphia: W.B. Saunders, p. 50.

7. Pugh RN, Murray-Lyon IM, Dawson JL *et al*. (1973) Transection of the oesophagus for bleeding oesophagealvarices. *Br J Surg*60(8), 646–649.

8. Christensen E, Schlichting P, Fauerholdt L *et al*. (1984) Prognostic value of Child–Turcotte criteria in medically treated cirrhosis. *Hepatology*4, 430–435.

9. Anthony PP, Ishak KG, Nayak NC *et al.* (1978) the morphologyof cirrhosis. Recommendations on definition, nomenclature, and classification by a working group sponsored by the World Health Organization. *J ClinPathol*31(5), 395–414.

10.Poynard T, McHutchison J, Manns M *et al.* (2002) Impact of pegylatedinterferon alfa-2b and ribavirin on liver fibrosis in patients with chronic hepatitis C. *Gastroenterology* 122(5), 1303–1313.

11.Wanless IR, Nakashima E, Sherman M (2000) Regression of humancirrhosis. Morphologic features and the genesis of incomplete septalcirrhosis.*Arch Pathol Lab Med* 124(11), 1599–1607.

12. G. D'Amico, G. Garcia-Tsao and L. Pagliaro, Natural historyand prognostic indicators of survival in cirrhosis: A systematic review of 118 studies, *J Hepatol***44** (2006), 217–231.

13.Kutami R, Girgrah N, Wanless IR, Sniderman K, Wong FS, Sherman M, et al. The Laennecgrading system for assessment of hepatic fibrosis: validation by correlation with wedged hepatic vein pressure and clinical features. Hepatology. 2000;32:407A.

14.Nagula S, Jain D, Groszmann RJ, Garcia-Tsao G. Histological-hemodynamic correlation in cirrhosis—a histological classification of the severity of cirrhosis. J Hepatol.2006;44:111–7.

15.Castera L. Non-invasive methods to assess liver disease in patients with hepatitis B or C. Gastroenterology. 2012;142:1293–302

16.Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portalpressure, presence of gastroesophagealvarices and variceal bleeding. Hepatology. 1985;5:419–24.

17. Groszmann RJ, Bosch J, Grace N, Conn HO, Garcia-TsaoG, Navasa M, et al. Hemodynamic events in a prospective randomized trial of propranolol vs placebo in the prevention of the first variceal hemorrhage. Gastroenterology. 1990;99:1401–7.

18. Vorobioff J, Groszmann RJ, Picabea E, Gamen M, Villavicencio R, Bordato J, et al. Prognostic value of hepatic venous pressure gradient measurements in alcoholic cirrhosis: a 10-year prospective study. Gastroenterology. 1996; 111:701–9.

19.Gines P, Quintero E, Arroyo V. Compensated cirrhosis: natural history and prognosis.Hepatology. 1987;7:122–8.

20. D'Amico G, Morabito A, Pagliaro L, Marubini E. Survival and prognostic indicators incompensated and decompensated cirrhosis. Dig Dis Sci. 1986;31:468–75.

21. Ripoll C, Groszmann R, Garcia-Tsao G, Grace N, Burroughs A, Planas R, et al. Hepaticvenous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. Gastroenterology. 2007;133:481–8.

22. Berzigotti A, Garcia-Tsao G, Bosch J, Grace ND, Burroughs AK, Morillas R, et al. Obesity is an independent risk factor for clinical decompensation in patients with cirrhosis. Hepatology.2011;54:555–61.

23. Planas R, Montoliu S, Ballestè B, Rivera M, Miquel M, Masnou H, et al. Natural history ofpatients hospitalized for management of cirrhotic ascites. ClinGastroenterolHepatol. 2006;4:1385–94.

24. Salerno F, Guevara M, Bernardi M, Moreau R, Wong F, Angeli P, et al. Refractory ascites: pathogenesis, definition and therapy of a severe complication in patients with cirrhosis. Liver Int. 2010;1:937–47.

25. Guardiola J, Xiol X, Escribà JM. Prognostic assessment of cirrhotic patients with refractory ascites treated with a peritoneovenous shunt. Am J Gastroenterol. 1995;90:2097–102.

26. Fernandez J, Navasa M, Planas R, Montoliu S, Monfort D, Soriano G, et al. Primary prophylaxisof spontaneous bacterial peritonitis delays hepatorenal syndrome and improves survival in cirrhosis. Gastroenterology. 2007;133:818–24.

27. Arvaniti V, D'Amico G, Fede G, Mansou P, TsochatzisE, Pleguezuelo M. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis.Gastroenterology. 2010;139:1246–56.

28. Salerno F, Gerbes A, Ginès P, Wong F, Arroyo V. Diagnosis, prevention and treatment of hepatorenalsyndrome in cirrhosis. Gut. 2007;56:1310–8.

29. Serstè T, Lebrec D, Vallà D, Moreau R. Incidence and characteristics of type 2 hepatorenalsyndrome in patients with cirrhosis and refractory ascites. ActaGastroenterol Belg. 2008;71: 9–14.

30. Zoli M, Merkel C, Magalotti D, Gueli C, Grimaldi M, Gatta A, et al. Natural history of cirrhoticpatients with small esophageal varices: a prospective study. Am J Gastroenterol.2000; 95:503–8.

31. North-Italian Endoscopic Club. Prediction of the first variceal hemorrhage in patients withcirrhosis of the liver and esophageal varices. A prospective multicenter study. N Engl J Med. 1988;319:983–9.

32. D'Amico G, Garcia-Pagan JC, Luca A, Bosch J. HVPG reduction and prevention of varicealbleeding in cirrhosis. A systematic review.Gastroenterology.2006;131:1624.

33. D'Amico G, de Franchis R. Upper digestive bleeding in cirrhosis. Post-therapeutic outcomeand prognostic indicators.Hepatology. 2003;38:599–612.

34. de Franchis R. Evolving consensus in portal hypertension. Report of the Baveno IV consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol.2005;43:167–76.

35. de Franchis R. Revising consensus in portal hypertension. Report of the Baveno v consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol. 2010;53:762–8.

36. Abraldes J, Villanueva C, Banares R, Aracil C, Catalina MV, Garcia-Pagan JC, et al. Hepatic venous pressure gradient in patients with acute variceal bleeding treated with pharmacologic and endoscopic therapy. J Hepatol. 2008;48:229–36.

37. Fattovich G, Stroffolini T, Zagni I, Donato F. Hepatocellular carcinoma in cirrhosis: incidenceand risk factors. Gastroenterology. 2004;127:S35–50.

38. N'Kontchou G, Paries J, Htar MT, Ganne-Carrie N, Costentin L, Grando-Lemaire V, et al. Risk factors for hepatocellular carcinoma in patients with alcoholic or viral C cirrhosis. ClinGastroenterolHepatol. 2006;4:1062–8.

39. Ioannau GN, Splan MF, Weiss NS, McDonald GB, Beretta L, Lee SP. Incidence and predictors of hepatocellular carcinoma in patients with cirrhosis. ClinGastroenterolHepatol. 2007;5: 938–45.

40.Infante - RivardC ,Esnaola S , Villeneuve J - P *et al.* Clinical and statistical validity of conventional prognostic factors inpredicting short - term survival among cirrhotics . *Hepatology*1987 ;**7** : 660 – 664 .

41. OlthoffKM , Brown RS , Delmonico FL *et al.* Summary report of a national conference: evolving concepts in liver allocation in the MELD and PELD era . *Liver Transpl.*2004 ;**10** : A6 – A22 .

42. Kim WR ,Biggins SW , Kremers WK *et al.* Hyponatremia and mortality among patients on the liver transplant waiting list . *N. Engl. J. Med.* 2008 ;**359** : 1018 – 1026 .

43. Bustamante J , Rimola A , Ventura P - J *et al.* Prognostic significance of hepatic encephalopathy in patients with cirrhosis . *J. Hepatol.* 1999 ;**30** : 890 – 895 .

44. ArmonisA , Patch D , Burroughs A . Hepatic venous pressure measurement: an old test as a new prognostic marker in cirrhosis? *Hepatology*1997 ;**25** : 245 – 248

45. MaddreyWC ,Boitnott JK , Bedine MS *et al* . Corticosteroidtherapy of alcoholic hepatitis .*Gastroenterology* 1978 ;**75** : 193 – 199 .

46. Carithers RL Jr ,Herlong HF , Diehl AM *et al* . Methylprednisolone therapy in patients with severe alcoholic hepatitis. A randomized multicenter trial .*Ann. Intern.*

Med .1989 ;**110** : 685 – 690

47. Bell H, Skinningsrud A, Raknerud N, et al. Serum ferritinand transferrin saturation in patients with chronic alcoholic and non-alcoholic liver diseases. J Intern Med 1994; 236: 315–22.

48. Fargion S, Mattioli M, Fracanzani AL, et al. Hyperferritinemia, iron overload, and multiple metabolic alterations identify patients at risk for nonalcoholic steatohepatitis. Am J Gastroenterol2001; 96: 2448–55.

49. Walker, et al. Serum ferritin concentration predicts mortality in patients awaiting liver transplantation. Hepatology 2010;51:1683-1691.

50.Arroyo V, Gines P, Gerbes AL, Dudley FJ, Gentilini P, Laffi G,et al.Definition and diagnostic criteria of refractory ascites and hepatorenalsyndrome in cirrhosis. Internation Ascites Club. HEPATOLOGY1996;23:164-176.

51. Runyon BA. AASLD practice guideline: management of adult patients with ascites due to cirrhosis. HEPATOLOGY 2004;39:841-856.

52. Wiesner R, Edwards E, Freeman R, Harper A, Kim R, Kamath P, et al.Model of end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology 2003;124:91-96.

53.Stuart KA, Fletcher LM, Clouston AD, Lynch SV, Purdie DM, Kerlin P, et al.Increased hepatic iron and cirrhosis: no evidence for an adverse effect on patient outcome following liver transplantation. HEPATOLOGY 2000; 32:1200-1207.

54. Kayali Z, Ranguelov R, Mitros F, Shufelt C, Elmi F, Rayhill SC, et al. Hemosiderosis is associated with accelerated decompensation and decreased survival in patients with cirrhosis. Liver Int 2005; 25:41-48.

55. Ruddell RG, Hoang-Le D, Barwood JM, Rutherford PS, Piva TJ, WatterDJ, et al. Ferritin acts as a proinflammatory cytokine via iron-independent protein kinase C zeta/nuclear factor kappa B-regulated signaling in rat hepatic stellate cells. HEPATOLOGY 2009; 49:887-900.

56.Manousou P, Kalambokis G, Grillo F, Watkins J, Xirouchakis E, PleguezueloM, et al. Serum ferritin is a discriminant marker for both fibrosis and inflammation in histologically proven non-alcoholic fatty liver disease patients. Liver Int 2011;31:730-739.

57. CodrutaVagu1, Camelia Sultana et al. Serum iron markers in patients with Chronic Hepatitis C Infection. Hepat Mon. 2013;13(10):e13136.

58. Kowdley KV, Belt P, Wilson LA, Yeh MM, Neuschwander-Tetri BA, Chalasani N, Sanyal AJ, Nelson JE. Serum ferritin is an independent predictor of histologic severity andadvanced fibrosis in patients with nonalcoholic fatty liver disease. *Hepatology* 2012; 55: 77-85.

59. Natasha Chandok, Gerald Minuk, Matias Wengiel, Julia Uhanova. Serum ferritin levels do not predict the stage of underlyingnon-alcoholic fatty liver disease. J Gastrointestin Liver Dis2012; Vol. 21 No 1: 53-58.

60. **Nelson JE**, Wilson L, Brunt EM, Yeh MM, Kleiner DE,Unalp-Arida A, Kowdley KV. Relationship between the pattern of hepatic iron deposition and histological severity in nonalcoholic fatty liver disease. *Hepatology*2011; **53**: 448-457

61. **Sorrentino P**, D'Angelo S, Ferbo U, Micheli P, Bracigliano A,Vecchione R. Liver iron excess in patients with hepatocellularcarcinoma developed on non-alcoholic steato-hepatitis. *JHepatol*2009; **50**: 351-357

62. **Tan TC**, Crawford DH, Jaskowski LA, Murphy TM, Heritage ML, Subramaniam VN, Clouston AD, Anderson GJ,Fletcher LM. Altered lipid metabolism in Hfe-knockout mice promotes severe NAFLD and early fibrosis. *Am JPhysiolGastrointest Liver Physiol*2011; **301**: G865-G876

63. **Dixon SJ**, Lemberg KM, Lamprecht MR, Skouta R, ZaitsevEM, Gleason CE, Patel DN, Bauer AJ, Cantley AM,Yang WS, Morrison B, Stockwell BR. Ferroptosis: an irondependent form of nonapoptotic cell death. *Cell* 2012; **149**:

1060-1072

ANNEXURE

ABBREVIATIONS

ACLF	Acute on Chronic Liver Failure
APASL	Asia Pacific Association of Study of Liver
AASLD	American Association Study Of Liver Disease
CTP	Child Turcott Pugh
EASL	European Association of Study of Liver
INR	International Normalised Ratio
IL	Interleukin
MDF	Maddrey's Discriminant Function
MELD	Model for End stage Liver Disease
HVPG	Hepatic vein pressure gradient
BMI	Body Mass Index
SBP	Spontaneous Bacterial Peritonitis
HRS	Hepatorenal Syndrome
H.E	Hepatic Encephalopathy
HCC	Hepatocellular Carcinoma
HBV	Hepatitis B Virus

HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
AUDIT-CAlcohol Use Disorders Identification Test	
ALT	Alanine Amino Transferase
AST	Aspartate Amino Tranferase
GGT	Gamma GlutamylTransferase
ROC	Receiver Operating Curve
PHG	Portal Hypertensive Gastropathy
UGI	Upper Gastrointestinal Tract
NAFLD	Non-Alcoholic Liver Disease
PT	Prothrombin Time
INR	InternationNormalised Ratio

Proforma

Name		IP no		D.O.A	
Age	+	Unit		D.O.Discharge D.O.Death	
Sex		Ward		Duration of stay	
Address			Diagnosis		
Phone No.					
History					
Jaundice			Altered sensorium		
Abdominal Distension			Hematemesis		
Pedal edema			Malena		
Oliguria			Weight loss		
Puffiness of face			Spontaneous bleeding		
Fever			Muscle cramps		
Anorexia			Cough		
fatigue			Breathlessness		
Constipation			Diet		
Diarrhea					
Native medication					
Past h/o jaundice			Tattooing		
Diabetes			Blood transfusion		
Smoking			Drug abuse		
Alcohol Duration Gm/day					
Tuberculosis					
Examination					

HE grade		Clubbing		PR	
Nutrition		Cyanosis		RR	
Height		Parotid swelling		Temp	
Weight		Gynaecomastia		BP Systolic	
BMI		Palmar erythema		Diastolic	
Anaemia		Scrotal swelling		Pulse pressure	
Icterus		Skin changes		Neck veins	
Pedal edema		Abd veins		CVS	
Ascites		Back veins		RS	
Umblical hernia		Caput medusae			
Splenomegaly		Hepatomegaly			
Investigation					
USG Abdomen Liver Size Echoes Ascites Spleen			Endoscopy		
PV Doppler			CXR		
			CRP		
Ascitic fluid culture Colour SAAG Cell count			SERUM FERRITIN		
			Blood culture		
CTP			Urine culture		
MELD		HBsAg		Steroids	
APACHE		HCV		pentoxyfylline	
SOFA		Anti HEV			
HRS		HIV			

Date					

TC					
Hb					
Platlet					
RBS					
Urea					
Creatinine					
Sodium					
Potassium					
Bilurubin TOT					
Direct					
Indirect					
SGOT					
SGPT					
ALP					
Protein					
Albumin					
Globulin					
PT					
INR					
ABG					
Lactate					

Remarks

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. Shujaath Asif .M,
PG in DM Medical Gastroenterology,
Department of Gastroenterology,
Madras Medical College,
Chennai-3.

Dear Dr. Shujaath Asif .M,

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Serum Ferritin – An Independent Prognostic Marker in Predicting Early Mortality in Advanced Liver Disease"** No. 36092013

The following members of Ethics Committee were present in the meeting held on 10.09.2013 conducted at Madras Medical College, Chennai-3.

1. Dr. G. Sivakumar, MS FICS FAIS	-- Chairperson
2. Prof. R. Nandini, MD Director, Instt. of Pharmacology, MMC, Ch-3	-- Member Secretary
3. Prof. Shyamraj, MD Director i/c, Instt. of Biochemsitry, MMC, Ch-3	-- Member
4. Prof. P. Karkuzhali, MD Prof. Instt. of Pathology, MMC, Ch-3	-- Member
5. Prof. Kalai Selvi, MD Prof. of Pharmacology, MMC, Ch-3	-- Member
6. Prof. Siva Subramanian, MD Director, Instt. of Internal Medicine, MMC, Ch-3	-- Member
7. Thiru. S. Govindasamy, BABL	-- Lawyer
8. Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

13/3/14

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003.

Member Secretary, Ethics Committee

13/3/14.

Information sheet

We are conducting a study on “Serum Ferritin – An Independent Prognostic Marker in predicting early mortality in Advanced Liver Disease” at The Department of Medical Gastroenterology, Rajiv Gandhi Govt General Hospital, Chennai. The purpose of the study is to know whether serum ferritin predicts early mortality in patients in Decompensated Chronic Liver Disease and Acute on Chronic Liver Failure.

The privacy of the patients in this research will be maintained throughout the study.In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time. Your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the study may be intimated to you at the end of the study period or during the study if anything is found abnormal. This may aid in the management or treatment.

Signature of Investigator Signature of participant

Date:

INFORMED CONSENT FORM

Title of the Study:

Serum Ferritin – An Independent Prognostic Marker in predicting Early mortality in Advanced Liver Disease

Name of the Participant:

_____

Name of the Investigator: Dr. ShujaathAsif.M

Name of the Institution : Madras Medical College.

Documentation of the informed consent

I _____ have read the information of this form (or it had been read to me). I was free to ask any questions and they have been answered. I hereby give my consent to be included as a participant in

Serum Ferritin – An Independent Prognostic Marker in predicting Early mortality in Advanced Liver Disease

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.

Name and signature / thump impression of the participant

Name _____ Signature _____ Date____

Name and signature of impartial witness (required for illiterate patients):

Name _____ Signature _____ Date____

Address and contact number of the impartial witness:

Name and signature of the investigator or his representative obtaining consent:

ஆராய்ச்சி தகவல் தாள்

சென்னை இராஜீவ்காந்தி அரசு பொது மருத்துவமனைக்கு வரும் நோயாளிகளில், கல்லீரல் நோயினால் பாதிக்கப்பட்டவர்கள் குறித்த ஆய்வு இங்கு நடைபெற்று வருகிறது.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க விரும்புகிறோம். இந்த ஆராய்ச்சியில் உங்களை பங்கேற்க வைத்து அதன் தகவல்களை ஆராய்வோம். அதனால், தங்களின் நோயின் ஆய்வறிக்கையோ, சிகிச்சையோ பாதிக்கப்படாது என்பதைத் தெரிவித்துக் கொள்கிறோம்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும்போதோ அல்லது ஆராய்ச்சின்போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

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ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

பங்கேற்பாளரின் உறவினர் கையொப்பம்

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு

"கல்லீரல் நோயினால் பாதிக்கப்பட்டவர்களைப் பற்றிய ஆய்வு"

ஆராய்ச்சி நிலையம் : இராஜீவ்காந்தி அரசு பொது மருத்துவமனை
சென்னை மருத்துவக்கல்லூரி,
சென்னை - 600 003.

பங்கு பெறுபவரின் பெயர் :

பங்குபெறுபவரின் எண் :

பங்கு பெறுவர் இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தகமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு இரத்தம், சிறுநீர், ஊடுகதிர் படம் மற்றும் மின் உடலியங்கியல் பரிசோதனை செய்துகொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி

ஆய்வாளரின் பெயர் .....

நோயாளியின் உறவினர்/காப்பாளர் கையொப்பம் ..... இடம் ..... தேதி

SERUM FERRITIN –AN INDEPENDENT PROGNOSTIC MARKER IN PREDICTING EARLY MORTALITY IN ADVANCED LIVER DISEASE

Dissertation submitted in partial fulfilment of requirements for

DM DEGREE IN MEDICAL GASTROENTEROLOGY

BRANCH IV

Of

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY,
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S.NO	NAME	GE . NO	AGE IN YEARS	SEX	JAUNDICE	ASCITES	ENCEPHALOPATHY	GRADE OF ENCEPHALOPATHY	FEVER	UGI BLEED	DIABETES	SMOKING	ALCOHOL	OTHER CAUSES
1	BALAN	1777/13	56	M	Y	Y	y	3	N	Y	N	Y	Y	N
2	SANTHANAM	2103/13	48	M	Y	Y	Y	3	N	Y	N	Y	Y	N
3	KUMUDHA	1724/11	27	F	Y	Y	Y	3	N	Y	N	N	N	HBV
4	VELU	7415/12	48	M	Y	Y	Y	3	N	Y	N	Y	Y	N
5	RAGHUPAT	734/12	56	M	Y	Y	Y	1	N	N	N	N	Y	N
6	PALANI	3930/13	43	M	Y	Y	Y	3	N	Y	N	Y	Y	N
7	SARAVANA	2267/13	36	M	Y	Y	Y	1	N	Y	N	Y	Y	N
8	GUNASEKA	4519/13	45	M	Y	Y	Y	3	N	Y	N	Y	Y	N
9	KUMAR	4718/13	40	M	Y	Y	Y	1	N	N	N	N	Y	HBV
10	GOVIND	489/13	34	M	Y	Y	Y	1	N	N	N	N	Y	N
11	RAJAGOPA	4571/13	38	M	Y	Y	Y	1	N	N	N	N	Y	N
12	RAJU	3890/13	43	M	Y	Y	Y	1	N	Y	Y	N	N	NAFLD
13	MUNUSAM	2294/13	50	M	Y	Y	Y	1	N	N	N	Y	Y	N
14	GOVINDAN	5047/13	51	M	Y	Y	Y	1	N	N	N	Y	Y	N
15	RAMESH	4098/13	46	M	Y	Y	Y	1	N	N	N	Y	Y	N
16	VADIVEL	4735/12	32	M	Y	N	N	N	N	N	N	N	Y	N
17	GUNALAN	4614/13	45	M	Y	Y	Y	1	N	N	N	Y	Y	HBV
18	THIRUPATH	3986/12	43	M	Y	Y	Y	1	N	N	N	N	Y	N
19	RADHAKRIS	4654/13	44	M	Y	Y	N	N	N	N	N	Y	Y	N
20	LOGANATH	4492/13	34	M	Y	Y	Y	1	N	N	N	Y	Y	N
21	RATHNAM	5364/13	34	M	Y	Y	Y	1	N	N	N	Y	Y	N

22	RATHNA KU	5677/12	45	M	Y	Y	Y	1	N	Y	N	Y	Y	N
23	MANOHAR	6798/13	47	M	Y	Y	Y	2	N	Y	N	Y	Y	N
24	ARUMUGA	5678/13	56	M	Y	Y	Y	3	N	Y	N	Y	Y	N
25	SANTHANA	2103/13	56	M	Y	Y	Y	1	N	Y	N	Y	Y	HCV
26	ARUMUGA	6837/13	45	M	Y	Y	Y	1	N	Y	Y	N	N	HBV
27	MANI	4567/12	45	M	Y	N	N	N	N	N	N	N	N	HCV
28	RAJ	6137/12	48	M	Y	Y	Y	3	N	Y	N	N	N	HBV
29	SHEIKH MO	4673/13	54	M	Y	Y	Y	3	N	Y	N	Y	Y	N
30	ALLAH BAK	5672/11	56	M	Y	Y	Y	4	N	Y	Y	Y	N	HBV
31	KARTHIK	3456/12	45	M	Y	Y	Y	3	N	Y	N	Y	Y	N
32	RAJA	5437/12	65	M	Y	Y	Y	1	N	Y	N	N	Y	HBV
33	JAGADISH	4563/13	44	M	Y	Y	Y	1	N	N	N	N	Y	N
34	SATHEESH	4785/12	39	M	Y	Y	Y	4	N	Y	N	N	Y	N
35	DEVENDRA	5133/13	54	M	Y	Y	Y	3	N	Y	N	Y	Y	N
36	RANI	6756/12	45	F	Y	Y	Y	3	N	N	Y	N	N	NAFLD
37	LAKSHMI	2564/11	67	F	Y	Y	Y	4	N	Y	N	N	N	HBV
38	MURUGAN	4785/11	54	M	Y	Y	Y	4	N	N	N	Y	Y	N
39	KONDAIYA	4414/13	50	M	Y	Y	Y	4	N	Y	N	N	Y	HBV
40	JEYARAM	1706/11	37	M	Y	Y	Y	1	N	Y	N	N	N	HCV
41	VENKATESA	6619/10	30	M	Y	Y	Y	1	N	N	N	N	Y	N
42	BALAMURT	3324/13	22	M	Y	Y	Y	1	N	Y	N	Y	Y	N
43	RAVI	6044/13	55	M	Y	Y	Y	4	N	Y	N	Y	Y	N
44	SARAVANA	6215/132	39	M	Y	Y	Y	4	Y	N	N	N	Y	HCV
45	PARASURA	6235/13	34	M	Y	Y	Y	1	N	N	N	N	N	HBV
46	MALA	1394/09	21	F	Y	Y	N	N	N	N	N	N	N	HCV
47	SRINIVASA	6315/12	54	M	Y	Y	N	N	N	Y	N	Y	Y	N
48	GOWTHAM	5400/13	56	M	Y	Y	Y	1	N	Y	N	Y	Y	N
49	NAGAPPAN	5997/13	47	M	Y	Y	Y	4	N	Y	Y	Y	Y	N
50	BALACHAN	5982/13	34	M	Y	Y	N	N	N	Y	N	Y	Y	N
51	PITCHANDI	6093/13	45	M	Y	Y	N	N	N	N	N	Y	N	HBV
52	SARBUDEE	4341/11	49	M	Y	Y	Y	3	N	Y	N	N	N	HCV
53	ARIF KHAN	3487/12	54	M	Y	Y	Y	4	N	Y	Y	N	N	NAFLD

54	SURESH	3258/13	30	M	Y	Y	N	N	Y	N	N	N	Y	N
55	ELANGO	1245/13	43	M	Y	Y	N	N	N	N	N	Y	Y	N
56	RAJI	324/10	43	F	Y	Y	N	N	N	Y	N	N	N	HBV
57	KARTHIBAN	2367/11	64	M	Y	Y	N	N	N	Y	N	N	Y	N
58	SURESH	3254/11	54	M	Y	Y	N	N	N	Y	N	N	Y	N
59	MALAIVAS/	4356/12	45	M	Y	Y	N	N	N	Y	N	N	Y	N
60	ANGAMUT	3456/10	47	M	Y	Y	Y	3	N	Y	N	N	Y	N
61	RAVI.G	6543/11	43	M	Y	Y	N	N	N	Y	N	N	Y	HBV
62	GUNAVATH	6688/13	45	F	Y	Y	Y	3	N	Y	Y	N	N	NAFLD
63	RANI	6548/10	56	F	Y	Y	Y	3	N	Y	N	N	N	HCV
64	SARITHA	4325/11	43	F	Y	Y	Y	3	N	Y	N	N	N	HBV
65	VENKATES/	4765/12	54	M	Y	N	N	N	N	N	N	Y	Y	N
66	KARUNANI	6543/10	65	M	Y	Y	N	N	N	N	N	N	Y	N
67	VARATHAR	109/14	56	M	Y	Y	N	N	N	N	N	N	N	NAFLD
68	KUMARAN	156/14	45	M	Y	N	N	N	N	N	N	Y	Y	N
69	RAVIKUMA	1234/14	46	M	Y	Y	Y	1	N	Y	N	N	Y	N
70	ELDER BON	213/14	50	M	Y	Y	Y	4	N	Y	N	Y	Y	N
			45.91429											

HEPATOMEGALY	SPLENOMEGALY	SPIDERNAEVI	WBC CELLS/Cu mm	HB in gm%	PLATELET COUNT IN LAC/CU.MM	RBS	BLOOD UREA	CREATININE	SERUM SODIUM	SERUM POTASSIUM	SERUM BILIRUBIN	AST	ALT
N	N	Y	8100	8.3	1.81	145	20	0.7	137	3.2	16.9	356	231
N	N	Y	11,000	10.6	1.7	156	21	0.8	137	3.2	13	6.2	384
N	N	Y	5500	6.5	0.7	134	22	0.7	134	3.2	11	386	286
Y	Y	Y	4900	8.3	2.5	148	21	0.8	136	3.6	6.5	354	275
Y	N	N	4400	7.1	0.7	135	22	0.9	136	3.8	4.1	124	134
N	N	Y	4400	8.8	0.65	143	45	2	122	2.4	13	454	420
N	N	Y	6000	6	0.7	135	37	1.7	122	2.6	14	565	467
N	N	Y	5800	8	0.75	129	22	2.3	134	3.6	12	254	235
N	N	Y	5600	8	0.8	125	24	0.9	134	3.5	13	345	324
N	N	Y	4500	8.9	0.7	127	30	3.5	141	4.1	14	280	260
N	N	Y	8000	9	1.2	137	34	3.2	141	3.3	3	128	126
Y	N	N	6000	9	1.1	245	22	3.5	136	4.2	8	458	468
N	N	Y	7800	6	0.5	145	34	1.7	122	2.5	6	565	543
N	N	Y	7000	9.8	1.2	124	22	0.7	134	3.7	6	256	234
N	N	Y	4900	9.9	0.6	110	38	0.9	141	3.1	6.4	342	245
N	N	N	6700	9	0.7	145	23	0.8	141	4.5	6	245	234
N	N	Y	6000	7	0.8	176	23	0.9	143	3.6	7	234	254
N	N	Y	5600	7	0.6	134	23	0.8	137	3.7	7	457	453
N	N	N	6000	8	0.8	134	21	0.9	138	3.5	5	234	123
Y	Y	Y	7000	10	1.2	134	23	0.9	137	3.4	6	126	135
N	N	Y	8000	9	1.2	156	23	0.9	145	3.6	5	345	234

N	N	Y	5600	6	0.8	134	23	0.7	136	3.7	5	245	234
Y	N	Y	7800	8	1.1	124	24	0.7	138	3.2	7	256	234
Y	Y	Y	6700	5	0.5	122	23	1.5	123	2.4	2	654	543
Y	Y	Y	4500	8	1.1	145	25	0.7	143	3.8	7	236	231
Y	Y	Y	5600	6	1.2	134	23	3.5	138	2.6	7	134	121
N	N	N	7890	11	0.9	145	34	3.5	145	4.2	6	345	321
N	N	N	8600	8	0.6	143	34	0.9	142	4.5	7	254	231
N	N	Y	5670	9.6	0.8	123	27	0.7	139	3.8	7	239	123
Y	Y	Y	4500	6	0.5	145	50	1.5	132	2.5	21	874	834
N	N	Y	5600	12	0.7	143	32	1.1	129	2.7	21	432	324
N	N	N	5400	8	1.2	145	28	0.9	134	2.7	7	342	236
N	N	N	7600	6	0.45	123	34	0.8	135	3.5	7	125	121
Y	Y	Y	6700	8	0.7	145	35	0.8	134	3.2	7	235	214
N	N	Y	6500	9.6	0.67	157	25	0.8	143	3.6	8	345	234
N	Y	Y	7800	8	1.1	145	34	0.8	145	3.7	7	234	212
N	N	N	11000	5	0.56	123	34	1.7	143	3.7	7	267	245
N	N	Y	13000	7	0.67	111	45	2.7	111	4.5	21	876	834
N	N	Y	7800	6	0.54	121	56	4.3	114	5.7	16	654	542
N	N	N	4500	12	0.78	134	22	0.7	36	4.5	5	223	212
N	N	Y	6700	9.7	1.4	123	23	0.8	138	4.2	6	432	345
N	N	N	4500	10.7	0.78	154	26	0.8	142	4.5	8	342	324
Y	Y	Y	7800	5	0.67	165	45	2.1	111	4.3	23	765	769
N	N	Y	5400	6	1.3	213	34	3.3	114	5.5	26	654	765
N	N	N	4500	13	1.5	123	23	0.6	143	4.3	4	234	224
N	N	N	9000	2	1.8	134	24	0.8	143	3.9	2	76	67
N	N	Y	5600	8	1.2	137	27	0.5	145	4.7	7	321	253
N	N	N	5700	8.6	0.76	148	25	0.6	142	4.1	5	435	345
Y	Y	Y	4300	8	0.45	111	25	0.8	142	4.6	14	234	213
N	N	Y	5200	13	0.75	125	26	0.7	137	3.7	18	432	378
N	N	N	7600	7	0.85	132	24	0.6	136	3.5	19	225	214
N	N	Y	5400	8.4	0.54	143	28	0.7	141	4.2	23	984	876
N	N	N	6500	7	0.45	123	34	3.2	123	2.4	25	784	654

N	N	Y	4500	8	0.67	134	23	0.6	145	3.7	15	342	256
N	N	N	7800	12	1.3	126	21	0.9	143	3.4	14	231	23
N	N	N	4300	7.4	0.45	132	21	0.6	142	3.6	21	211	207
N	N	Y	6700	12	0.8	154	28	0.9	143	4.2	24	894	765
N	N	Y	5400	8	0.67	134	34	4.2	145	4.3	21	674	543
N	N	Y	5500	9	0.56	123	34	1.7	139	4.4	17	453	432
N	N	Y	4500	7	0.67	154	23	0.7	143	4.5	17	345	321
N	N	Y	5600	9	0.87	143	23	0.8	138	3.2	21	567	543
N	N	N	7600	8	0.75	134	23	0.8	139	3.5	16	453	345
N	N	N	4700	8	0.65	145	23	0.8	137	3.6	18	348	212
N	N	N	7600	12	0.87	154	27	0.9	138	3.6	17	342	321
N	N	N	7600	14	1.6	154	32	0.9	145	4.6	2	43	34
N	N	N	7800	8	0.9	143	23	0.9	139	4.7	3	65	54
N	N	N	6700	8	0.76	143	23	0.7	136	4.2	17	109	111
N	N	N	8700	9	0.67	143	23	0.9	143	3.8	4	78	56
N	N	N	4500	8	0.56	156	24	0.7	143	4.2	13	109	123
N	N	Y	4500	6	0.78	165	34	2.3	32	2.6	21	456	654

ALP	PROTEINS	ALBUMIN	PT	INR	VARICES	PHG	SBP	BLOOD CULTURE	OTHER INFECTIONS	D.F < 32	D.F > 32	CTP UPTO 6	CTP 7-9
232	6.9	3.5	22.6	1.66	Y	Y	N	N	N	N	Y	N	N
364	129	6.1	20.6	1.45	Y	Y	N	N	N	N	Y	N	N
210	5.8	2.8	22	1.6	Y	Y	N	N	N	N	N	N	N
224	5.8	2.4	24	1.8	Y	Y	N	N	N	N	Y	N	N
100	5.7	2.2	21	1.5	N	N	N	N	N	N	Y	N	N
124	5.6	2.2	35	2.5	Y	Y	Y	N	N	N	Y	N	N
123	5.3	2.1	21	1.5	Y	Y	N	N	N	N	Y	N	N
108	5.9	2.4	21	1.4	Y	Y	N	N	N	N	Y	N	N
108	5.6	2.2	20	1.4	Y	Y	N	N	N	N	Y	N	N
89	5.4	2.2	13	1.01	Y	Y	N	N	N	N	Y	N	N
67	6.2	3	14	1.02	Y	Y	N	N	N	Y	N	N	Y
209	6.2	3.2	31	2.48	Y	Y	N	N	N	N	N	N	N
210	5.3	2.1	32	1.7	Y	Y	N	N	N	N	Y	N	N
98	5.9	2.9	19	1.5	Y	Y	N	N	N	N	Y	N	N
112	5.6	2.2	28	3.17	Y	Y	N	N	N	N	Y	N	N
89	6	3.4	24	1.5	Y	N	N	N	N	N	Y	N	N
123	5	2.7	26	1.7	Y	Y	N	N	N	N	Y	N	N
123	6.1	3.4	25	1.9	Y	Y	N	N	N	N	Y	N	N
78	6.3	3.7	14	1.01	N	N	N	N	N	Y	N	N	Y
90	6	3	13	1.01	Y	Y	N	N	N	Y	N	N	Y
123	5.2	2.3	21	1.7	Y	Y	N	N	N	N	Y	N	N

122	5.7	2.5	21	1.6	Y	Y	N	N	N	N	Y	N	N
109	6	2.4	21	1.8	Y	Y	N	N	N	N	Y	N	N
103	5.4	2.2	25	1.7	Y	Y	N	N	N	N	Y	N	N
108	5.8	2.4	21	1.6	Y	Y	Y	N	N	N	Y	N	N
78	6	2.4	19	1.56	Y	Y	N	N	N	N	N	N	N
99	6	3.6	13	1.03	N	N	N	N	N	N	N	Y	N
108	5.2	2.5	24	1.89	Y	Y	N	N	N	N	N	N	N
78	5.4	2.4	24	1.56	Y	Y	N	N	N	N	Y	N	N
154	5	2.1	26	2.56	Y	Y	Y	N	N	N	N	N	N
122	5	2.5	23	1.5	Y	Y	N	N	N	N	Y	N	N
111	6.4	3.6	13	1.01	Y	Y	N	N	N	Y	N	N	Y
89	5.4	2.7	23	1.87	Y	Y	N	N	N	N	Y	N	N
90	5.7	2.4	21	1.9	Y	Y	Y	N	N	N	Y	N	N
102	6	2.9	21	1.9	Y	Y	N	N	N	N	Y	N	N
109	7	3.2	25	2.78	Y	Y	N	N	N	N	N	N	N
101	5.4	2.2	27	2.67	Y	Y	N	N	N	N	N	N	N
107	5.2	2.2	28	2.89	Y	Y	Y	N	N	N	Y	N	N
112	5.3	2.1	32	2.89	Y	Y	N	N	N	N	Y	N	N
108	5.6	2.5	21	1.76	Y	Y	N	N	N	N	N	N	N
87	5.7	2.6	21	1.87	Y	N	N	N	N	N	Y	N	N
111	6	3.2	27	2.4	Y	Y	N	N	N	N	Y	N	N
112	5.3	2.1	34	3.14	Y	Y	N	N	N	N	Y	N	N
134	5.3	2.5	32	2.9	Y	Y	Y	N	N	N	Y	N	N
87	6	2.9	14	1.04	Y	N	N	N	N	N	N	N	Y
98	6.7	3.7	13	1.01	N	N	N	N	N	N	N	Y	N
117	5.6	2.4	28	2.79	Y	Y	N	N	N	N	Y	N	N
102	5.2	2.3	25	1.4	Y	Y	N	N	N	N	Y	N	N
101	5.3	2.1	25	1.67	Y	Y	N	N	N	N	Y	N	N
88	5.1	2.3	29	1.9	Y	Y	N	N	N	N	Y	N	N
101	5.4	2.4	26	1.72	Y	Y	N	N	N	N	N	N	N
106	5.1	2.1	34	2.89	Y	Y	N	N	N	N	N	N	N
112	56	2.2	34	2.9	Y	Y	N	N	N	N	N	N	N

101	5.6	2.5	23	1.78	Y	Y	N	N	N	N	Y	N	N
89	5.9	2.3	23	1.8	Y	Y	N	N	N	N	Y	N	N
76	5.3	2.1	24	2.1	Y	Y	N	N	N	N	N	N	N
123	5.6	2.1	25	2.6	Y	Y	N	N	N	N	Y	N	N
111	5.9	2.7	25	2.1	Y	Y	N	N	N	N	Y	N	N
111	5.6	2.5	23	1.7	Y	Y	N	N	N	N	Y	N	N
234	5.9	3	25	2.1	Y	Y	N	N	N	N	Y	N	N
123	6	3.2	21	1.67	Y	Y	N	N	N	N	Y	N	N
102	5.8	2.6	18	1.5	Y	N	N	N	N	N	N	N	N
200	5.9	3.2	21	1.6	Y	N	N	N	N	N	N	N	N
127	6	3.4	26	1.9	Y	Y	N	N	N	N	N	N	N
109	6.4	3.6	13	1	N	N	N	N	N	N	N	Y	N
78	6.4	3.8	13	1.01	N	N	N	N	N	Y	N	Y	N
98	6.2	4	15	1.1	Y	N	N	N	N	N	N	N	Y
89	6	3.5	13	0.9	N	N	N	N	N	Y	N	Y	N
145	6	3	17	1.5	Y	N	N		N	N	Y	N	N
145	5.3	2.1	27	1.6	Y	Y	N	N	N	N	Y	N	N

CTP >10	MELD UPTO 9	MELD 10 -19	MELD > 20	MELD	SE. FERRITIN , 200 ng/ml	SE.FERRITIN 200 - 400 ng/m/	S.FERRITIN >400 ng/ml	OUTCOME	SURVIVAL < 15 days	SURVIVAL > 15 days	CAUSE OF DEATH	SERUM FERRITIN IN ng/ml	
Y	N	N	Y	24.6	N	N	Y	D	Y	N	MOF	629	
Y	N	N	Y	28.6	N	N	Y	D	Y	N	MOF	567.6	
Y	N	N	Y	22.8	N	N	Y	D	Y	N	MOF	941	
Y	N	N	Y	21.4	N	N	Y	D	Y	N	MOF	662.2	
Y	N	N	Y	26.5	Y	N	N	A	N	Y		106	
Y	N	N	Y	25	N	N	Y	D	Y	N	MOF	447.7	
Y	N	N	Y	28	N	N	Y	D	Y	N	MOF	2045	
Y	N	N	Y	23.6	N	N	Y	D	Y	N	MOF	736.9	
Y	N	N	Y	22.5	N	N	Y	D	Y	N	MOF	1034	
Y	N	N	Y	23.4	N	Y	N	A	N	Y		356	
N	N	Y	N	15.6	Y	N	N	A	N	Y		36	
Y	N	N	Y	24.8	N	N	Y	D	Y	N	MOF	1471	
Y	N	N	Y	34	N	N	Y	D	Y	N	MOF	957	
Y	N	N	Y	27.5	Y	N	N	A	N	Y		112	
Y	N	N	Y	25.4	N	N	Y	D	Y	N	MOF	967	
Y	N	N	Y	23.2	Y	N	N	A	N	Y		133	
Y	N	N	Y	29.8	Y	N	N	A	N	Y		36.8	
Y	N	N	Y	24.2	Y	N	N	A	N	Y		67	
N	Y	N	N	7.6	Y	N	N	A	N	Y		107	
N	Y	N	N	8.4	Y	N	N	A	N	Y		145	
Y	N	N	Y	24	N	Y	N	A	N	Y		312	

Y	N	N	Y	27.5	N	N	Y	D	Y	N	MOF	668	
Y	N	N	Y	26.4	Y	N	N	A	N	Y		33.9	
Y	N	N	Y	34.7	N	N	Y	D	Y	N	MOF	1229.8	
Y	N	N	Y	35.6	Y	N	N	D	Y	N	MOF	137	
Y	N	N	Y	27.5	N	N	Y	D	Y	N	MOF	774	
N	Y	N	N	8.4	Y	N	N	A	N	Y		143	
Y	N	N	Y	29.4	N	N	Y	D	Y	N	MOF	1654	
Y	N	N	Y	29.8	N	N	Y	D	Y	N	MOF	986	
Y	N	N	Y	23.7	N	N	Y	D	Y	N	MOF	876	
Y	N	N	Y	22.4	N	N	Y	A	N	Y		321	
N	N	Y	N	16.5	N	N	Y	A	N	Y		765	
Y	N	N	Y	24.7	N	N	Y	A	N	Y		654	
Y	N	N	Y	23.4	N	N	Y	D	Y	N	MOF	1098	
Y	N	N	Y	32.4	N	N	Y	D	Y	N	MOF	2134	
Y	N	N	Y	26	Y	N	N	A	N	Y		67	
Y	N	N	Y	31.3	N	N	Y	D	Y	N	MOF	1876	
Y	N	N	Y	26.3	N	N	Y	D	Y	N	MOF	1654	
Y	N	N	Y	32.6	N	N	Y	D	Y	N	MOF	976	
Y	N	N	Y	27.4	N	Y	N	D	N	Y		245	
Y	N	N	Y	28.5	N	N	Y	D	Y	N	MOF	879	
Y	N	N	Y	25.3	N	N	Y	A	N	Y		783	
Y	N	N	Y	24	N	N	Y	D	Y	N	MOF	2063	
Y	N	N	Y	26	N	N	Y	D	Y	N	MOF	1256	
N	N	Y	N	18.4	N	Y	N	A	N	Y		321	
N	Y	N	N	6.4	Y	N	N	A	N	Y		56	
Y	N	N	Y	23.5	N	Y	N	D	Y	N	MOF	234	
Y	N	N	Y	26	N	Y	N	A	N	Y		45	
Y	N	N	Y	21	N	N	Y	D	Y	N	MOF	764	
Y	N	N	Y	32.6	N	Y	N	A	Y	N	MOF	313	
Y	N	N	Y	28.7	N	Y	N	A	N	Y		276	
Y	N	N	Y	24.7	N	N	Y	A	Y	N	MOF	843	
Y	N	N	Y	27	N	N	Y	D	Y	N	MOF	1876	

Y	N	Y	N	15.7	N	Y	N	A	N	Y		369	
Y	N	Y	N	17.4	Y	N	N	A	N	Y		54	
Y	N	N	Y	28	N	Y	N	A	N	Y		389	
Y	N	N	Y	24.5	N	Y	N	A	N	Y		264	
Y	N	N	Y	36.7	N	N	Y	A	N	Y		2063.3	
Y	N	N	Y	34.6	Y	N	N	A	N	Y		8.8	
Y	N	N	Y	28.5	N	Y	N	A	N	Y		290	
Y	N	N	Y	25.6	N	N	Y	A	N	Y		1160	
Y	N	Y	N	12.8	N	Y	N	A	N	Y		265	
Y	N	N	Y	29.6	Y	N	N	A	N	Y		132	
Y	N	N	Y	27.8	N	Y	N	A	N	Y		276	
N	Y	N	N	7.4	Y	N	N	A	N	Y		45	
N	Y	N	N	7.8	N	N	Y	A	N	Y		2654	
N	N	Y	N	17	N	Y	N	A	N	Y		102	
N	Y	N	N	7.4	N	Y	N	A	N	Y		377	
Y	N	Y	N	16.9	N	Y	N	A	N	Y		245	
Y	N	N	Y	28	N	N	Y	D	Y	N	MOF	1524	
												608.0281	

KEYS TO MASTER CHART

M	MALE
F	FEMALE
Y	YES
N	NO
A	ALIVE
D	DEAD
MOF	MULTI-ORGAN FAILURE
HBV	HEPATITIS B VIRUS
HCV	HEPATITIS C VIRUS
NAFLD	NON-ALCOHOLIC FATTY LIVER DISEASE